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A MODIFICATION IN THE ROUTINE TREATMENT OF SYPHILIS.

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Ehrlich's amplification of the discovery of the value of the organic salts of arsenic in the treatment of syphilis led to a wave of optimism. These first high hopes have not been fulfilled, further experience having proved that "arseno-benzol" is by no means the specific drug of which all are in search. In spite of this disappointment these new compounds have a certain value, and this value is undoubtedly great, in that a more rapid disappearance of symptoms has been effected. Further research led to the production of the "Neo" salts. It is true that these have eliminated a ponderous apparatus; but a more important point is the fact that they are less toxic to the patient, although they have failed to attain the complete elimination of the many complications consequent on the intravenous administration of arsenic. Of these complications the most serious is death, and, although the frequency of this sequel has been somewhat diminished, it has by no means been rendered negligible. Death as a direct result of therapeutical measures should be unknown. To this end experience and knowledge have been gradually garnered, with the result that patients suffering from cardiac and renal disease are now

treated with great circumspection. Despite their exception, however, the list of fatalities lengthens.

The object of this paper is to demonstrate a modification in the routine treatment of syphilis, whereby complications are almost entirely eliminated without in any way impairing the efficiency of the end-results.

Insistence must be made on the paramount importance of the "quantitative Wassermann" in the development and continuation of the modified routine here described. Equally important is the fact that the reaction must be performed by a thoroughly competent pathologist.

The Modification.

Instead of frequent small doses of novarsenobillon, a minimum of three injections of 0·9 grm. is given, the interval between each being at least three weeks. The majority of early cases give a negative Wassermann reaction twenty-one days after the final dose. At each injection a specimen of blood is taken and tested quantitatively, the effect of each injection thus being observed. Many cases give a negative reaction before the completion of the course, but the minimum number of injections is nevertheless administered. Should the test not prove satisfactory the intravenous therapy is continued until a negative reaction is attained. The longer period between infection and the commencement of treatment the greater is the difficulty in obtaining a clear blood test. In consequence the later cases receive a larger number of injections regulated according to the clinical signs, as a favourable Wassermann is but rarely obtained.

To revert to the early cases. Very few require more arsenic than is administered during the first two months of treatment. Occasionally a "muddy" reaction does appear in the serum after a few months, but further injections are then given at once, with invariably good results.

Mercury is given immediately a definite diagnosis is formed and is continued throughout the whole period of treatment, there being no intermissions at all other than such as may be necessary owing to stomatitis, etc. It is supplied in the form of a tablet consisting of hyd. c̄ cret. gr. j, which is given by mouth three times a day.

Once the Wassermann reaction has become negative the patient is

given the mercury continuously for at least one year. During this year frequent tests are performed and the patient is kept under careful observation. When the reaction has been clearly negative for at least twelve months all treatment is stopped. The test is now applied every six weeks for a further year. Should this prove continuously negative during the whole of this period of probation, a lumbar puncture is performed and the cerebro-spinal fluid is examined. This is subjected to all the tests for syphilis, and on its proving satisfactory the patient is discharged as cured. It is, of course, understood that no suspicious clinical signs have supervened during the two years.

Discussion.

Before proceeding to consider the question of arseno-therapy, which is the most important point in the modification here described, brief reference must be made to one or two other points in the treatment.

There is no doubt that inunction, when carried out thoroughly, is the best method of administering mercury—a method obviously impossible in the out-patient department.

It is true that intra-muscular injection is painful and may lead to local abscess formation, but a more important contra-indication to this method is the fact that the mercury may become loculated, as proved by Cole and Littman(1), who demonstrated this possibility by means of X-rays. Should such occur, not only has the patient failed to absorb the metal, but he is liable to traumatic rupture of several loculi, acute mercurial poisoning being the result.

A bottle of medicine is more inconvenient for daily use than is a tablet and so is rarely used. It may well be argued that the patient may not take his pills, and over this there is no control other than definite and reasoned admonition. Experience has proved that the normal patient appreciates the importance of the mercury and does do his best to help himself.

No reference has so far been made to the iodide of potash. It is frequently given in the later manifestations where gummatous infiltration is present; in these conditions it has its value, and is accordingly used in conjunction with the mercury and arsenic. A few cases

showing intense œdema around the primary sore have also obtained benefit from its use, this condition having subsided but slowly under ordinary treatment, thus confirming the statements of Wilfrid Fox. One curious fact has emerged as a result of the use of the iodide. When the following mixture is prescribed the improvement in the clinical condition of cases showing late cutaneous manifestations is very marked:

R.

Pot. iod.	gr. x
Hydrarg. biniod.	gr. $\frac{1}{16}$
Inf. cinch. ac. ad.	℥j

M. ft. mist.

Whitfield first noticed that the acid infusion of cinchona seems to be essential to this amelioration. Control cases placed on the same mixture differing merely in the vehicle do not show such rapid progress. This effect may be due to the larger amount of alkaloid in the acid infusion; although quinine has dropped out of memory in modern therapeutic methods it was used exclusively and extensively for many years in France.

The question of lumbar puncture has been brought very much to the fore by those enthusiasts who would test the cerebro-spinal fluid of every syphilitic patient immediately on his entry to hospital. But where is the advantage of this procedure? Even if the fluid should give a positive reaction in an early case would it modify the treatment in any detail? Kinnear Wilson maintains that intravenous therapy would even then be the wiser course, reserving intrathecal medication for the later cases. There is then no value in the operation from a therapeutical point of view. There is no need to submit the patient to the possible discomfort of severe headache. There is no need to penetrate the dura mater, thus causing a local trauma which might well prove the starting-point of a syphilitic meningitis. It is true that definite knowledge of early neural infection may be lost. In reply it can only be stated that a positive reaction in the fluid of an early case who has undergone the whole period of treatment and observation has never been found among those attending the clinic, therefore it would not seem advisable to increase the risk of neuro-syphilis as a result of early lumbar puncture.

The question of the neosalvarsan compounds is more complicated,

the differing opinions of many authorities being reflected in the numerous variations in the method of administration. In 1918 Whitfield and Emery were much impressed by the fact that death never followed a first injection, but always occurred subsequent to a second or later dose. Willcox was at that time working on the excretion of arsenic, and proved that one month elapses before the whole of any one intravenous injection is completely removed from the body. The amount remaining at the end of three weeks, however, is so small as to be negligible.

In view of this discovery the danger would seem to be the possibility of accumulation. For these reasons Whitfield suggested that a longer interval should be allowed to elapse between successive administrations of arsenic, and that twenty-one days between each injection should be the minimum. The maximum single dose which could be given with safety was at that time unknown; therefore the earlier work under this scheme was largely occupied with the search for the optimum quantity.

More recent work by Foulerton has to some extent explained the delay in the appearance of symptoms of salvarsan poisoning. He has proved that the injected arsenic is "fixed" to a fat molecule, the compound thus formed being carried to the liver, where it is dealt with but slowly. Excessive accumulation might lead to hepatic degeneration—a hypothesis borne out by post-mortem examination. Mackenzie Wallis([2]) has recently proved that the greatest effect of hepatic damage occurs three months after the last dose of arsenic.

From these facts it would seem reprehensible to increase the possibility of the accumulation of arsenic. This is becoming more generally recognised, for Harrison([3]) has declared himself convinced that careful observation of the patient throughout the whole of the course is of great importance in the avoidance of severe toxic effects, whilst Willcox([4]) has recently definitely stated that fatal cases following treatment with salvarsan are probably much more frequent than is commonly supposed.

Many authorities give frequent injections of gradually increasing strength. In many cases only two days elapse between successive doses, whilst in others the longest interval is only one week. This is a type of treatment only too commonly carried out, and by this method it is absolutely impossible to form any estimate whatever of

the total amount of arsenic present in the body at any one stated period. Dangerous accumulation must occur.

It might well be argued that a dose of 0·9 grm. of novarsenobillon is in itself perilously large. Clinical experience has proved this to be well borne, however, whilst larger doses have given rise to anxiety. But in the use of so large an injection the three weeks' interval assumes a great importance.

One further point might be mentioned, though it is possibly only of minor moment. There is no biological reason why the *Treponema pallida* should be unable to emulate the horse in the acquisition of immunity. Thus by starting with small doses of salvarsan and then giving frequent and gradually increasing doses, it is conceivable that the organism may even become immunised to the drug.

It is desirable to give the maximum amount of the drug possible in order to produce a cure as speedily as is possible, but in so doing all danger to the patient must be avoided. Therefore the standard of treatment evolved is 0·9 grm. of novarsenobillon at three weekly intervals. Further, observation has proved that in early cases three such injections suffice to render the Wassermann reaction negative.

Five Hundred Cases.

Although some two thousand patients have attended the clinic since 1918, it is only possible to consider about five hundred of them for various reasons. In the first place many were treated during the period of evolution of this modification, and so cannot be said to have undergone the method of treatment here described. In the second place many others have attended very irregularly, despite all endeavours to impress upon them the importance of strict observance of all instructions. Others have removed from the district and so have been transferred to other centres. Some have been treated by other methods and other drugs, such as sulfarsenol and silver-salvarsan. Lastly, age, cardiac and renal disease have necessitated the administration of but small doses of novarsenobillon to many patients.

The "Primary" Cases.

The following tables demonstrate the results attained more briefly and clearly than would be otherwise possible.

Table I shows that only 11 cases out of a total of 139 fail to approach the standard at which the modification aims. Seven of these cannot justly be deemed failures, as 5 of them are known to have omitted mercury for periods varying from three to six months, whilst the remaining 2 cases had slight but suspicious albuminuria, and so were treated rather less strenuously—that is, 4 cases only show definite failure. The histories of these are interesting and are worthy of inclusion.

TABLE I.

No. of cases showing—		Females.	Males.	Total.
Spirochætes present in lesion. Blood never "positive"		0	17	17
Negative reaction in blood after 1 injection		15	20	35
„ „ „ 2 injections		14	26	40
„ „ „ 3 „		6	16	22
„ „ 3 months after 3rd injection		1	4	5
„ „ 6 „ „		1	1	2
„ „ after more than 3 injections (average No. 5·28)		1	6	7
Blood still giving a positive reaction } definite failures		0	1	1
Definite relapses whilst under treatment } definite failures		0	3	3
Doubtful „ „ „		3	4	7
Total numbers		41	98	139

No. 572 : This man had a preputial chancre in February, 1919, and although the usual treatment was carried out, the Wassermann reaction in the blood never became negative. The primary lesion rapidly disappeared and no further clinical signs appeared until late in 1920, when extensive necrosis of the vomers and maxillæ supervened simultaneously with an increase in the strength of the Wassermann. Further injections have cleared this up, but the positive reaction in the blood still persists.

No. 661 : In September, 1919, a hard sore was found on the glans penis. This rapidly vanished under treatment, although the positive reaction in the blood persisted with some variations in its strength. Despite continuous mercury and repeated courses of injections late lesions appeared on the forehead and scrotum early in 1921. It is true that this case had been somewhat complicated by the presence of an intense intestinal toxæmia.

These two patients prove that reliance can be placed on the

Wassermann reaction; that continuous positive reports presage the appearance of late lesions at some time or other. This definite statement is further borne out by the two remaining failures.

No. 701: This man attended the clinic in December, 1919, with great preputial necrosis and suppurating buboes. Repeated examinations for the spirochæte proved negative, whilst his Wassermann did not become even weakly positive until three months had elapsed. Since its appearance, however, it has been remarkably persistent, treatment continuous, strenuous and varied, having no effect upon it. Since the end of 1920 numerous late syphilitic lesions have become evident, whilst their resolution has been but slow.

No. 874: A man who, in April, 1920, first attended with a hidden chancre and extensive local necrosis. Despite all treatment since the Wassermann has remained faintly positive, although no signs or symptoms have hitherto appeared.

These last two cases are suggestive in that they were the most serious cases of œdema and necrosis seen at the clinic. They may have been infected by a particularly virulent strain of spirochæte, but the fact remains that a negative reaction has never been attained, whilst one of them has since shown late lesions.

Table II demonstrates the varying periods for which the remaining 128 patients have been observation:

Table II.

No. of cases having undergone at least—	Females.	Males.	Total.
9 months' treatment and observation	12	27	39
12 ,, ,, ,,	6	10	16
15 ,, ,, ,,	0	5	5
18 ,, ,, ,,	7	17	24
24 ,, ,, ,,	13	31	44
Total	38	90	128
9 months' probation	1	4	5
12 ,, ,,	12	27	39
Total	13	31	44

All of these cases have answered the requirements of the modification, whilst 44 patients have been definitely discharged as cured.

Table III shows Tables I and II expressed in percentage form, with the omission of the seven doubtful cases of relapse.

Table III.

No. of cases who showed—	Total.	Per-centage.
Negative reaction 3 months after 3rd injection and have continued so to do	119	90·1
„ „ 6 months after 3rd injection and have continued so to do	2	1·5
„ „ after 4 injections and have continued so to do	4	3·0
„ „ „ 6 „ „ „	1	0·7
„ „ „ 7 „ „ „	1	0·7
„ „ „ 8 „ „ „	1	0·7
Continuously positive reaction	1	0·7
Definite relapse	3	2·2
Total	132	99·6

Briefly then, the actual percentage failure is only 3, and this figure is at least as good as that obtained by any other type of routine treatment. It is true that many have not yet been discharged as cured, but they have reacted satisfactorily to all tests as far as possible.

The "Secondary" Cases.

These patients commence treatment even later, three months from the date of infection being the average period during which the spirochætes have been given opportunity to flourish. It is therefore to be expected that the results attained among these cases are not so good as among those showing the earlier lesions. Table IV bears out this fact, demonstrating that 23 out of a total of 146 have failed to reach the requisite standard.

Table IV.

No. of cases showing—	Females.	Males.	Total.
Negative reaction in blood after 1 injection	8	4	12
„ „ „ „ 2 injections	21	21	42
„ „ „ „ 3 „	24	9	33
„ „ „ 3 months after 3rd injection	5	5	10
„ „ „ 6 „ „ „	4	0	4
„ „ „ after more than 3 injections (average number = 4·5)	11	11	22
Blood still giving a positive reaction } Definite failures	2	1	3
Definite relapses whilst under treatment } Definite failures	5	5	10
Doubtful „ „ „	7	3	10
Total numbers	87	59	146

But of these failures ten are known to have omitted mercury for

intervals varying from three to twelve months. Excluding these delinquents there remain 13 patients who have not fulfilled expectations.

No. 664: A male who first attended in October, 1919. His blood has constantly given a positive reaction despite all treatment, whilst clinically leukoplakia has supervened.

Nos. 633 and 680: In these women infection occurred simultaneously with conception. During pregnancy their Wassermann reactions became negative and continued so until after the birth of the children, who by the way are quite healthy, since when positive results have been continuous.

Nos. 718 and 792: The blood of these women advanced from negative to faintly positive whilst they were taking mercury. This phenomenon proved merely transitory, however, the tablets sufficing to re-establish and maintain negative reactions.

A similar sequence of events occurred with two men, Nos. 777 and 852.

Nos. 818 and 1156: These men returned a definitely positive reaction in the blood two months after entering on probation, but neither signs nor symptoms were evident. Subsequent treatment has remedied the matter, as it has also done in No. 851, a woman whose Wassermann was unsatisfactory six weeks after the cessation of all treatment.

One female patient, No. 653, returned a positive reaction shortly after being told to continue on mercury alone. She refuses further injections and now attends very irregularly. As she suffered no ill-effects after the salvarsan and is of curious mentality it would seem extremely doubtful whether she has ever taken the tablets regularly.

No. 1030: This man acquired syphilis at the age of sixty. All apparently went well for six months, at the end of which period his blood suddenly returned to positive. Within four weeks there occurred a cerebral thrombosis with resultant hemiplegia and death.

No. 822: A woman who reacted well to treatment for six months. She then became pregnant and ceased attending, only to return a year later with a positive Wassermann and a child showing signs of congenital syphilis. Subsequent treatment, particularly strenuous during a succeeding pregnancy, has resulted in the birth of a healthy infant and an apparent cure in the mother.

These failures again prove the value of the Wassermann reaction

in that a positive test frequently precedes the appearance of signs. This was particularly marked in Nos. 644 and 1030.

Table V demonstrates the periods for which the remaining 123 satisfactory patients have been under observation.

Table V.

No. of cases having undergone at least—	Females.	Males.	Total.
9 months' treatment and observation . . .	28	13	41
12 „ „ „	12	12	24
15 „ „ „	4	1	5
18 „ „ „	8	8	16
24 „ „ „	21	16	37
Total . . .	73	50	123
9 months' probation	10	3	13
12 „ „	14	14	28
Total . . .	24	17	41

By this it is seen that 28 patients have answered all the tests at the end of twelve months' probation whilst another 13 are apparently destined to emulate them.

Table VI gives the results shown in Tables IV and V in the form of percentages, whereby it is seen that the failures number 9·5 per cent. This figure, too, is quite as good as that obtained by other variations in the treatment of "secondary" syphilis.

Table VI.

No. of cases who showed—	Total.	Per-centage.
Negative reactions 3 months after 3rd injection and have continued so to do	97	71·3
„ „ 6 months after 3rd injection and have continued so to do	4	2·9
„ „ after 4 injections and have continued so to do	14	10·2
„ „ „ 5 „ „ „ „	6	4·4
„ „ „ 6 „ „ „ „	1	0·7
„ „ „ 7 „ „ „ „	1	0·7
Continuously positive reaction	3	2·2
Definite relapse	10	7·3
Total	136	99·7

Discussion on the Cases of "Early" Syphilis.

Absolute certainty as to whether or no these cases are definitely and permanently cured is, of course, impossible. Observation during the next forty years is the only means of settling that question.

That modern therapy is of some value may be presumed from the fact that the out-patient department of to-day no longer contains large numbers of men and women showing extensive gummatous infiltration and ulceration. Such cases are now exceedingly rare—a fact which points to the efficiency of the recent methods of treatment in early cases. Mercury and iodide of potash are still used in dealing with gummata, but they alone cannot have attained so marked a result so suddenly.

A point which is not adequately appreciated to-day concerns the exhibition of mercury. Mercury is essential in the warfare on syphilis, as is shown by the large number of patients who omit to take the tablets and who later return to the clinic with symptoms, signs, or a positive Wassermann. Among the cases here considered are the seventeen problematical failures, all of whom are known to have neglected repeated admonitions on the subject.

That the standard of cure established in this modification is of some value is proved by the fact that only three cases—Nos. 818, 851 and 1156—have returned a positive Wassermann during the period of probation, and these relapses have all occurred within the first two months. Therefore it would seem that one year's close observation after the cessation of treatment is sufficient.

Definite proof of cure is but rarely possible and the two following cases are therefore worthy of note. The first is a conclusive case of re-infection.

No. 1412: This man, then aged 45 years, first attended hospital on May 19th, 1921. He gave a history of a hard sore in the preceding January. In May the scar could be seen in the sulcus, whilst there was also present a generalised rash of grouped follicular papules together with marked tonsillar ulceration and universal adenitis. Needless to say the Wassermann reaction was strongly positive. He underwent the routine course of treatment, his blood becoming negative after the second injection of novarsenobillon. He ceased attendance in August, 1921, only to reappear on February 2nd, 1922, with an undoubted chancre on the prepuce together with typical shotty glands in the groin. Spirochætes were found in the lesion, although the blood test proved negative on that day. Owing to the history and to the fact that the site of the lesion excluded a relapsing chancre, treatment was not commenced at once. On February 16th

the Wassermann become faintly positive, whilst the 22nd of the month saw the appearance of a typical generalised papulo-macular rash with faucial ulceration. This second infection has reacted normally to treatment.

The second case is that of a woman—No. 880—who first attended in January, 1920. This was about ten weeks after infection and she showed an ordinary secondary eruption. With her she brought a child, six weeks old and having a syphilitic papular rash. Both gave strongly positive Wassermann reactions. The mother was submitted to the usual course of treatment, answering all tests satisfactorily, but in September, 1920, she again became pregnant and the problem of further treatment was thereby rendered more difficult. However, it was considered that mercury given throughout the whole of pregnancy should suffice as she came under observation shortly after infection. A child was born in June, 1921, and up to the age of twelve months has shown neither signs of congenital syphilis nor a positive blood test. Immediately after parturition the mother was put on probation and has answered all tests satisfactorily during the last year.

These early cases of syphilis form the class which is of such great importance from the point of view of public health, and for that reason the percentage of failures must be as low as possible. Absolute efficacy of treatment has not yet been attained, though it can be claimed that the figures given by this modification are at least as good as those resulting from any other variety of treatment—this with less trouble both to the practitioner and to the patient.

In support of this assertion, it would perhaps be more valuable to quote a few figures from recent papers.

Fildes and Parnell, in the Medical Research Council's Special Report, No. 41, give the following results of treatment with six doses of "914" each of 0·45 grm. at intervals of three days, no mercury at all being administered :

Of 44 men with chancres and negative blood reactions 39 still showed negative Wassermanns four months after treatment, whilst the remaining 5 were all definitely re-infected.

Of 128 men with chancres and positive blood reactions 7 showed clinical relapses, 16 had persistently positive Wassermanns and 5 had induced negative reactions return to positive. That is a failure of 21 per cent. Observation extended over four months.

Of 144 men with "secondary" eruptions the corresponding figures were 9, 18 and 8—a failure of 23 per cent.

Of 29 men who came under treatment at least one and a-half years after infection 21 had persistently positive reactions during the four months' observation, *i. e.* a failure of 72 per cent.

Among 22 "primary" cases who were also given some mercury there were 6 failures, whilst 44 "secondary" cases under similar conditions contained 9 failures.

Mackenzie(5) gave a year's mercurial treatment with 6 doses of 0·3 grm. of "606" at weekly intervals at the commencement. Eighty-four "primary" cases were followed for one year, and at the end of that period 9 still gave positive reactions. In identical circumstances 658 "secondary" cases showed 134 with positive Wassermanns and 64 clinical recurrences. The percentage failures are therefore 10 and 30.

A comparison with these results speaks for itself.

Neurosyphilis.

Late syphilis presents rather a different problem in that a complete cure cannot be expected; even an apparent freedom from the disease is but rarely attained. Therefore the object of treatment is to remove symptoms and to prevent progress of the lesion. It is impossible to "cure" the central nervous system if that is heavily scarred as a result of the spirochætal invasion.

Table VII indicates that not one of all the cases treated can be discharged as requiring no further supervision.

Table VII.

No. of cases showing—	Females.	Males.	Total.
A Wassermann reaction which is still positive (Group I) .	6	34	40
„ „ „ now negative (Group II) .	3	8	11
Total . . .	9	42	51
Average number of months' treatment in Group I . .	19·3	11·0	12·3
„ „ „ „ II .	33·0	26·0	27·9
„ injections in Group I . . .	5·1	3·2	3·5
„ „ „ II . . .	7·3	4·6	5·5

It is noteworthy that eleven patients now return a negative Wassermann reaction in the blood, which is equivalent to a percentage of 26·8 of all cases treated. Not one of these tests, however, has been

negative for more than six months. If this period be deducted from the total duration of attendance it is seen that these people have received about double the amount of medication that has been given to those in Group I.

This would suggest that negative tests can be obtained in the serum if only treatment be sufficiently persistent.

Many authorities maintain that intravenous therapy has no value whatever in neurosyphilis. Direct refutation of that statement is provided by the following case:

No. 164: This woman first attended the clinic in 1918 showing the typical signs and symptoms of tabes dorsalis, the Wassermann, both in the blood and cerebro-spinal fluid, being strongly positive. At the time lightning pains formed her chief complaint. Novarsenobillon was administered according to the usual routine, the immediate effect of each injection being an acute exacerbation of the pains. The end of the course of salvarsan saw the complete disappearance of all symptoms whilst the blood test gave a perfectly clear negative result. Continuous ingestion of mercury by mouth did not prevent a return of the lightning pains at the end of three months, the Wassermann now proving to be strongly positive once more. Arsenic was given in the same form and in the same manner as at the beginning of her treatment, and with identical results, both as regards the serum reaction and the increased intensity of the symptoms within two hours of the injection. This cycle has now been repeated three times, the case being the most stubborn of all the neurosyphilides that have come under observation.

The fact remains that although it is impossible to claim a cure in any one of these patients, every one of them has improved clinically to a great extent and the majority of them show absolute cessation of advance in the march of the disease. Whilst it is possible to obtain such definite results by the intravenous method of salvarsan administration, it seems unnecessary to expose the patient to the dangers consequent on intrathecal treatment.

Late Lesions in the Skin and Mucous Membranes.

Table VIII condenses the histories of some eighty cases, all of whom bore the later stigmata of syphilis either in the form of gummatous laryngitis, palatal ulceration, leukoplakia or cutaneous lesions.

Table VIII.

No. of cases showing—	Females.	Males.	Total.
A Wassermann reaction which is still positive (Group I) .	26	35	61
„ „ „ now negative (Group II).	5	14	19
Total . . .	31	49	80
Average number of months' treatment in Group I . .	17·5	18·7	18·2
„ „ „ „ II .	26·8	19·8	21·6
„ injections in Group I . . .	4·1	4·4	4·3
„ „ „ II . . .	6·0	4·0	4·5

In contra-distinction from the corresponding sections among those showing lesions of the central nervous system, Groups I and II here reveal no striking divergence between their respective periods of attendance. The contrast is more evident when it is realised that no Wassermann reaction has been negative for more than six months in any member of the second division. Therefore it is impossible to prophesy with regard to the effects of prolonged application to treatment, although without exception all cases have responded well from a purely clinical point of view, only 31·1 per cent. now giving a negative blood test.

The frequency with which mercurial stomatitis occurred among these patients was curious.

The explanation may lie in the fact that most of them are of middle age, and, perhaps in consequence of this, have either marked pyorrhœa or dental caries.

Laryngeal involvement necessitated careful consideration and some reduction in the dosage of novarsenobillon owing to the very real danger of the Jarisch-Herxheimer phenomenon, this being an acute focal congestion immediately consequent on the injection. One case only gave rise to anxiety as a matter of fact, yet it had the effect of producing a reluctance to give high doses in these patients. For that reason the standard of 0·9 grm. of N.A.B. was not rigidly maintained in ten of the above eighty cases.

Latent Syphilis.

The term "latent" is here used as describing parents who have no luetic signs themselves, yet whose blood gives a positive result to the Wassermann test, and whose children show undoubted congenital

lesions or whose family histories of repeated miscarriage first led to the reaction being carried out.

Some fifty-nine such cases have come under observation, 57·6 per cent. of these returning a negative Wassermann after twenty months' treatment. The results are indicated in Table IX.

TABLE IX.

No. of cases showing—	Females.	Males.	Total.
A Wassermann reaction which is still positive (Group I) .	14	11	25
,, ,, ,, now negative (Group II) .	23	11	34
Total . . .	37	22	59
Average number of months' treatment in Group I . .	17·7	21·0	18·8
,, ,, ,, ,, II .	20·8	20·0	20·3
,, injections in Group I . . .	4·8	4·0	4·4
,, ,, ,, II . . .	3·0	2·1	2·7

Although the two groups do not differ widely in the total periods of attendance, the difference between the relative strengths of their reactions is evident. This in spite of the fact that no marked divergence can be found either in the histories or in the clinical response to treatment. Neither signs nor symptoms of old infection have become manifest among any of the patients.

The women are of much greater importance than the men, in that they may convey congenital lues to their children, and therefore all are treated strenuously throughout the whole duration of pregnancy. At first injections were discontinued during the ninth month, but further experience taught that they can be given right up to the last day without any danger of producing abortion. The urine is of course very closely watched in case nephritis should appear. The Wassermann reaction in the blood is now entirely disregarded during the whole of the gestation period as a result of one disaster.

No. 497: Shortly after conception this woman was found to give a negative result to the blood test and for that reason she was allowed to continue on mercury alone. The Wassermann was continuously negative until shortly after labour, when increasingly positive reactions were returned. She gave birth to a syphilitic child.

The difference between this case and that quoted above—No. 880—lies in the duration of the infection. Whereas No. 497 had acquired syphilis many years before, No. 880 was an early case. Therefore

mercurial treatment alone during pregnancy was deemed sufficient in the latter patient—a view confirmed by the birth of a healthy infant and the mother's subsequent history.

The Wassermann reaction during pregnancy is undoubtedly a snare, negative results being almost the rule. The sequel to labour is a return to positive in practically all these older cases, yet persistent treatment does produce apparently good and permanent effects, as instanced by No. 612.

This woman, who gave a history of a secondary rash some five years before, attended regularly and went through the whole course of treatment, including the twelve months' probation. Since then she has given birth to a healthy child.

Excellent results are therefore attained among this type of patient in that healthy children are the invariable result of prolonged treatment. This must be carried out during the whole of gestation, and the Wassermann reaction must be entirely disregarded if it has been positive immediately previous to conception.

Congenital Syphilis.

Table X.

No. of cases showing—	Females.	Males.	Total.
A Wassermann reaction which is still positive (Group I) .	10	9	19
„ „ „ now negative (Group II).	3	3	6
Total . . .	13	12	25
Average number of months' treatment in Group I . .	25·8	19·3	22·7
„ „ „ „ II .	23·6	22·6	23·1
„ injections in Group I . . .	6·0	4·1	5·1
„ „ „ II . . .	2·6	0·6	1·6

The majority of these cases were young children, and in consequence the maximum dose of neosalvarsan was variable and calculated according to the age of the infant.

Of the twenty-five patients treated at the hospital all have attended for about two years, but only 31·5 per cent. now give a negative Wassermann reaction. Although this fact does not lead to undue optimism the clinical results are far more encouraging. Provided that the spirochætes have not caused extensive damage to a vital organ before their presence is suspected, death but rarely ensues once

treatment has been thoroughly undertaken, whilst the advance of nearly all lesions is at once checked if this be sufficiently strenuous. Many already extensive areas of destruction are repaired to a surprising extent. Thus, an interstitial keratitis leaves only minute traces behind if treated whilst in its early stages.

Of all the varying types of lesion the following give the best results clinically: arthritic changes, periostitis, interstitial keratitis and all cutaneous changes.

Choroiditis and deafness are improved to some extent. One boy, a case of infantilism, has not reacted to treatment at all.

No. 1735 is interesting in that she is now aged 36 years and has brought up a family of three boys, all of whom are absolutely healthy, whilst she herself is a bad case of congenital syphilis.

In brief it may be said that despite the fact that most of these cases seem to do excellently, the Wassermann reaction most commonly remains steady and is but little reduced in strength. There seems to be no correlation between the test and the clinical aspect of the case.

Complications.

In considering the complications directly consequent on arsenical treatment it is necessary to review all the cases that have attended the clinic since 1918, owing to the fact that many have arisen in patients whose histories could not be included here owing to very irregular attendance, etc.

Close on two thousand men and women have been treated, whilst the total number of injections given approximates five thousand.

During the year 1919 a rule was made that every patient must be admitted to hospital for at least one night. This arrangement allowed complete observation of temperature, pulse, etc., together with a more careful search for cardiac or renal disease. It was at that time realised that a damaged kidney might well become inflamed as a result of its endeavours to excrete arsenic, whilst definite heart trouble would more easily predispose to syncope, particularly if a Jarisch-Herxheimer reaction should occur in the neighbourhood of a sclerotic coronary artery with resultant complete occlusion of the vessel.

The patient was admitted to the ward at 10 a.m. and was allowed

no food until 3 p.m., the injection being given at 1.30 p.m. This "partial starvation" rule resulted from a short experience in 1918, when it was found that vomiting nearly always occurred if the patient had a full stomach at the time at which the arsenical compound was given.

Among the otherwise healthy cases thus treated there occurred the following complications:

(*a*) Nausea and vomiting within two minutes of the injection, three cases.

(*b*) Erythema chiefly around the joints appeared in one woman twelve hours after the first injection. After the second dose it was more marked, and was yet more obvious after the third. The end-result was good and no sign of hepatic disease ever appeared.

(*c*) Immediate collapse of short duration: Three cases exhibited this phenomenon and are of some interest. The first occasion on which this symptom appeared was in a woman who had declared her fear of the sight of blood. Unfortunately she caught sight of the test-tube, in which there was being collected a specimen for transmission to the laboratory. At once her face became livid, with leaden-hued lips, whilst her pulse at the wrist was fluttering and almost impalpable. Subsequent injections were given without any ill-effect whatsoever, great care having been taken that the woman should not see any blood. This incident lent some weight to the contention that this type of complication is of psychic origin. This hypothesis was effectually exploded a few weeks later by the second case.

This man had had several previous injections of novarsenobillon. On one occasion neokharsivan was administered owing to the fact that supplies of the former drug had given out. The patient was not told of the change and could not possibly detect it himself, but within ten seconds of the intravenous injection he exhibited symptoms similar to those shown by the woman. In his case, too, subsequent doses of novarsenobillon were administered without any untoward symptoms resulting.

The third patient to cause uneasiness in this way was a woman who had previously had but one injection. Reasoning from experience in the first two cases she was given a third dose in spite of the symptoms which had occurred at the second injection. Unfortunately she again

exhibited similar phenomena, and so it was deemed wise to desist from further intravenous treatment. A possible explanation for her behaviour could not be found.

(*d*) The "nitritoid" crisis. Two patients during 1919 first demonstrated the so-called "nitritoid" crises. One minute after the injection the face is seen to flush and the veins stand out prominently. A slight bronchitis with consequent cough appears. Dyspnœa is concurrent, and sometimes approaches an asthmatic attack so marked is it. Diarrhœa may occur. No reason for the appearance of these symptoms could be found among the patients, though it seems possible that a hyper-sensitiveness may occur in these people as among asthmatics. One physician at King's College Hospital, who is unfortunately an asthmatic, frequently gets an attack of sneezing, bronchitis and dyspnœa if he should happen to inhale any of the powdered novarsenobillon.

(*e*) One patient complained of a taste of garlic within a few seconds of the administration of the arsenical compound, whilst one other described a metallic astringency in his mouth.

Experience during 1918, 1919 and 1920, therefore, yielded some eleven cases of complication, and but few patients having proved a source of anxiety, it was felt that it would be safe to inject some cases in the out-patient department. To this end instructions were given to the patients concerned as to fasting. Among the group so treated the following complications occurred :

(*a*) Nausea and vomiting, four cases.

(*b*) "Nitritoid" crises, two cases.

(*c*) Collapse, one case.

This man got up and walked home immediately after the injection, despite firm instructions to rest quietly for two hours. He collapsed about a mile from the hospital and was brought in by a L.C.C. ambulance. Careful inquiry elicited the fact that he had starved himself for the twenty-four hours immediately preceding his visit to the clinic. He has since been given further injections with no apparent ill-effect.

This group of patients therefore yields a list of seven complications.

The years 1921 and 1922 have seen a marked reduction in the incidence of nausea and vomiting. This as a result of the discovery that most of the patients exhibiting these phenomena were markedly

constipated. Of those cases who vomited several have since had injections without the slightest trace of nausea resulting, great care having been taken to secure an efficient action of the bowels on the morning of the injection.

Reducing the matter to figures Table XI shows the total percentage of complications to be only 0·36.

TABLE XI.

Type of complications among—	In-patients.	Out-patients.	Total.	Percentage among 5000 injections.
Taste of garlic	1	—	1	0·02
Metallic taste	1	—	1	0·02
Nausea and vomiting	3	4	7	0·14
Nitritoid crisis	2	2	4	0·08
Erythema	1	—	1	0·02
Collapse	3	1	4	0·08
Total	11	7	18	0·36

Of all the eighteen cases only four have been serious—those of collapse. Even of these more grave cases but one remains unexplained, whilst all have recovered.

Two last facts must be mentioned. No case of jaundice has ever been reported, nor has one ever been traced. Among the deaths that have occurred from intercurrent disease, etc., not one is even suspicious in that it might possibly have been the result of treatment.

A brief review of some other figures may here be inserted. Fildes and Parnell (*loc. cit.*) mention 1250 cases involving 6588 injections. Fifty-five of these patients suffered from complications, *i.e.* a percentage of 4½. There were actually some 170 complications of various types, many of which occurred in the same patient. Therefore reducing these to the absolute minimum by counting the number of cases (55) and contrasting this with the number of injections there still remains a percentage of 0·83.

Chamberlain (6) notes 54 cases of jaundice among a total of 1200 patients who had been treated with salvarsan. Novarsenobillon was used in 552 cases and jaundice occurred in 19 of these—a percentage of 3·4.

Harrison (7) noted diarrhœa in 1·8 per cent., vomiting in 6·9 per cent., and headaches in 17·4 per cent. of his second series of cases.

Conclusion.

The organic compounds of arsenic, although not possessing the specificity at one time claimed for them, are yet of undoubted value. The almost miraculously rapid disappearance of signs and symptoms in any early case, consequent on their use, must not be allowed to overshadow the essential importance of continuous mercurial administration. Nor must it be forgotten that the salvarsan group itself is not without danger to the patient. It is claimed that the method of administration here described reduces this danger to a minimum without in any way impairing the efficiency of the treatment. The rate of excretion of arsenic must be considered and its accumulation avoided if it is desired to eliminate all possibility of disaster.

Postscript.—Since these results were worked out a further 42 early cases have successfully attained the tentative standard of cure here described, whilst no failures of any kind have become evident.

References.

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(2) Mackenzie Wallis.—*Brit. Med. Journ.*, February 25th, 1922, p. 312.
(3) Harrison.—*Ibid.*, September 24th, 1921, p. 480.
(4) Willcox.—*Ibid.*, December 3rd, 1921, p. 945.
(5) Mackenzie.—*Glas. Med. Journ.*, June, 1919.
(6) Chamberlain.—*Lancet*, April 15th, 1922.
(7) Harrison.—*Diagnosis and Treatment of Venereal Disease in General Practice*, 1919.

It is with feelings of very deep regret that we have received the news of the death of Dr. J. J. Pringle, on December 18th last, while on a visit to New Zealand. His death will be a great loss to British Dermatology, and his cheery personality will be sorely missed by a large circle of friends.

A NOTE ON MOLLUSCUM CONTAGIOSUM.*

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Surgeon to the Hampstead and Royal National Orthopædic Hospitals.

For the material on which my observations have been made I am indebted to many dermatologists, beginning in 1894 with Mr. (now Sir) Malcolm Morris, who placed in my hands for pathological examination some typical specimens of lesions freshly excised. Since that now remote date I have lost no opportunity of observing the behaviour of the characteristic molluscum corpuscles when placed in surroundings that allow it to be shown whether they are living things.

The object of this paper is to induce others who, having command of material, have also time and inclination to repeat and extend, or to correct my observations.

The necessary apparatus need not occupy more than a square foot of space in a consulting room, and cannot but be pleasing to the eye, two pairs of Petri dishes being all that is required besides the microscope, slides and covers, mounted needles, wire loop, etc., which already find their places.

The patient's skin should be cleansed with absolute alcohol, no strong antiseptic being used. Water† should be taken after the tap has been allowed to run a few seconds, in order to remove traces of copper, and boiled, as also should be all watch-glasses, Petri dishes, slides, etc.

A watch-glass is placed in the lower of each pair of dishes, and some water (not enough to float or cover the watch-glass) is poured into the lower dish (*see* Fig. 1). One dish is left covered by its upper half; in the watch-glass contained in the other is placed a little heap of excised lesions cut open from the surface downwards, or of the white wax-like material that can be obtained from ripe lesions by lateral pressure. For small portions a cupped slide raised

* Paper read before the Section of Dermatology, Royal Society of Medicine, on June 15th, 1922.

† I have had no opportunity of making cultures with rain-water, which might suit better than tap-water. Other variations of the culture medium will suggest themselves as worth trial. I have found that streaming occurs with normal saline, and the addition to the latter of a trace of bicarbonate of soda favours subdivision of the bodies into sub-equal segments.

above water-level by two other slides being placed under it may replace the watch-glass. A few drops of water, but not enough to cover the heap, are now added, and the upper dish is inverted over the lower.

The culture must be kept at room temperature, because incubation favours the growth of bacteria, which, when over-abundant, kill the specific parasites. Occasionally a culture apparently free from bacteria is obtained, but usually bacteria are present; in moderate number they do not prevent vital changes from occurring.

It is important to make clear drawings of objects at the time they appear under the microscope, and it assists the eye if the main features of each stationary part are traced by means of a drawing eye-piece or other similar optical instrument.

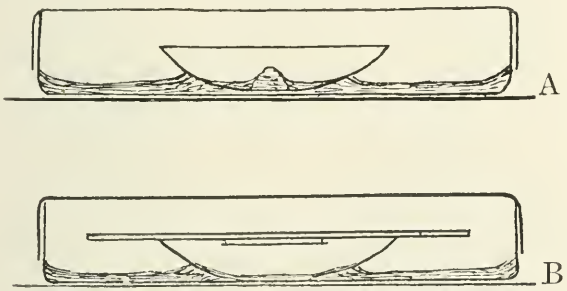

FIG. 1.—A, the material to be cultivated is heaped into the middle of a watch-glass; and water, but not enough to cover it, has been added drop by drop; B, after teasing in a drop of water on a slide a particle or drop of the material in "A" is covered and examined microscopically, then inverted over a watch-glass containing water and put between Petri dishes for re-examination later.

Enumeration of vital changes.—Some vital changes which I have already observed are shown in Fig. 2. They are (1) streaming of protoplasm with reproduction by budding; (2) formation of a supporting framework and of protective capsules; (3) formation of bird's-eye bodies; (4) vacuolation with oscillation of granules: (5) formation of active flagellate or spirillar bodies.

One of my latest observations was made in November, 1919, on material kindly provided by Dr. G. Pernet, Physician in Charge of the Department for Diseases of the Skin at the West London Hospital, and the House-Surgeon, Dr. Barker. I have also to thank Dr. Beverland and Mr. H. K. Shaw, Resident Medical Officers at the Hampstead General Hospital, for helping me with the preparations.

The specimens were placed in covered Petri dishes, some in tap-water as described above, others on spent tea-leaves in water.

All the preparations gave positive results. I was able to demonstrate the movement on the third, fourth, fourteenth and fifteenth days to seven different trained observers. In these demonstrations the movement was shown under a magnification of 500 diameters with a dry objective. The oil-immersion lens when used for preparations simply mounted in water has the drawback of dragging on the cover-glass and causing movements in the object beneath it, but it must be used to study certain features.

The preparations from Dr. Pernet's case I last examined on the thirty-fifth day after making the cultures. On this occasion streaming was present in a few only of the corpuscles, and the rest were obviously degenerating and becoming stained by the colouring matter of tea-leaves on which they were placed. So long as they remain in full vitality they do not absorb the colouring matter from the tea-leaves.

(1) *Streaming.*—The reality of the phenomenon being thus established a few details may be added. Fig. 2 (*a*) shows the aspect of a corpuscle just before streaming begins; its texture becomes more granular: this is succeeded by a disappearance of granules from either part of, as at (*b*), or throughout a corpuscle, as at (*c*), (*e*) and (*f*). The fresh corpuscle often presents indications of being segmented, and a regular segmentation is sometimes seen in water cultures; in one such I found the rotary motion affected one only of the segments, Fig. 2 (*d*). There are no separate granules to be seen in the moving substance, which must be composed of extremely minute elements,* but large granules are sometimes seen on the surface of the flowing part of a corpuscle; such granules I have observed to be carried round one segment of bodies such as those shown in Fig. 2 (*c*). Thus it appears to me that the phenomenon is a real streaming of protoplasm; at any rate it is conspicuous and quite different in aspect from effects produced by bacteria, motile or stationary.

Budding.—From some of the bodies with streaming protoplasm

* The uniform and all but homogeneous appearance of the streaming substance is quite in harmony with the filtrability of the fresh corpuscles after they have been ground up with sand and suspended in saline solution.

part of this can be seen to protrude, as in Fig. 2 (*f*), and in the neighbourhood are smaller spheres with streaming: in some of the latter there is a bright outer zone with no streaming. Some of the small streaming spheres have a vacuole. All three kinds when they are observed to come to rest assume a uniform retracting appearance and have a green tint. Although I have not seen the actual separation of one of these smaller bodies, after watching protrusions such as are shown in Fig. 2 (*f*) and (*g*), I have no doubt that they are formed by budding from the large bodies.

(2) *Doubly-contoured capsules* are rare in fresh material, but many develop in water-cultures, Fig. 2 (*c*). They seem to be formed as a

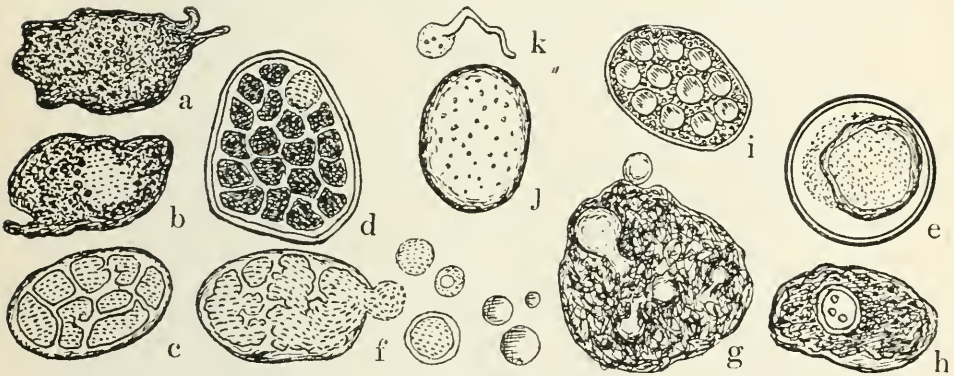

FIG. 2.—*a*, Molluscum body unchanged except that the cortex is more definite and the granules are larger; *b*, a clear area has formed and in it the protoplasm is circulating; *c*, an internal framework continuous with the cortex has formed and the whole of the protoplasm is circulating; *d*, a capsule has formed and within it the protoplasm is subdivided into segments, in only one of which the protoplasm is circulating; *e*, a spherical capsule has formed, the protoplasm is circulating and is in part protruded beyond the cortex; *f*, the whole protoplasm is circulating and a small protrusion is present, and there are three separate subdivisions with circulating protoplasm, one vacuolated, another with a clear outer zone, and, to the right, three subdivisions as they appear when they come to rest, clear and refracting; *g*, a body in which five subdivisions are seen in process of formation by budding; *h*, a body in which a nucleus-like structure has formed; *i*, a body with vacuolated protoplasm, the intervening granules in Brownian movement; *j*, a body with violent agitation of protoplasm; *k*, flagellated body with agitated granules at its expanded end. *d*, *f*, and *g*, × 800; the rest × 500.

defence against bacteria; I have seen many with bacteria on the outside of the capsule but never inside.

(3) *Internal framework.*—Irregular processes extending inwards may be formed apparently in the spaces between the segments of a

corpuscle. They are sometimes regular and anastomose to form a net, fig. 2 (*c*), or the framework* may be scanty as at (*f*).

(4) *Nucleus-like bodies.*—These are not present in the fresh corpuscle. Granules appear in an area where a nucleus or bird's-eye body is to be formed. Oscillating motion may be seen among the granules as the nucleus appears in a clear space bounded by a membrane. This stage represents, in my opinion, a low state of vitality of the molluscum body.

(5) *Vacuoles.*—These I have seen once as sketched in Fig. 2 (*i*). The granules between the vacuoles were in a state of oscillation or Brownian movement. I have seen a similar appearance in a sclerotium of that much-studied and interesting protist *Badhamia utricularis* after it had been twelve hours in water.

(6) *Flagellate bodies.*—This striking feature I have only once observed in a culture on the fourth day. The material was from abundant lesions, some of which I heaped up in the hollow of one of the cupped slides for hanging-drop preparations, and placed in a moist chamber as shown in Fig. 1. The result I described in the *Centralblatt für Bakteriologie*, 1895, i, p. 245.

The description, slightly condensed, runs:

"The most remarkable appearance consists in the presence of a great number of actively-moving flagellate bodies. They have a roundish head of the size of a red blood corpuscle, and a single powerful flagellum, and under a one-twelfth immersion lens were easily seen and unmistakable; many passed across the microscopic field and then escaped from sight. Many of the molluscum bodies were unchanged; of others, but a thin shell remained; still other had apparently undergone a liquefaction in their central part, and in this area were numerous highly-refracting oscillating granules."

I may add that in what I called the heads of the motile bodies (*see*

* In material given me by Dr. Ernest Dore last year I tested for cellulose some of the bodies in which a framework had formed by adding a few drops of a mixture of iodine solution (one part) to sulphuric acid (two parts). Parts of the framework changed to a greenish-blue colour, as much reaction as I have ever found in the fungal cellulose of moulds, mildews, etc. With the same reagent the molluscum bodies changed to a deep purple which lasted a few days, and the epithelial cells became pale yellow and swelled to oval form. Some *Synchytrium taraxaci* I treated in the same way and found its capsules were unaffected; the sporangial contents became dark green.

Fig. 2 (*k*)), there were oscillating particles quite like those present in those of the molluscum bodies I described as liquefied in the middle. The room in which the culture was made, in March, would be at a temperature not much above freezing at night, and for some hours each day somewhat above blood-heat, the preparation being placed on a chimney-piece above a bright fire.

The "heads" may be only residual, the flagellum becoming independent as a spirochæte or spirillum. I regard this state of reproduction as the acme of vitality in the cultivated parasite, the streaming state with budding coming next.

Answer is sure to be desired to one question: "Suppose we do as you suggest and see changes such as you describe, and even agree that they prove that the molluscum body is a parasite; in what biological text-book can we find an account of other parasites of the same genus?"

Taxonomy has no group in which we can find place for this parasite for which I have proposed the name *Plassomyxa contagiosa*.

Natural history still has some blank pages: one of these I am now asking you to help to fill.

Many have tried to identify the molluscum body with the familiar genus *Coccidium*. That attempt has failed.

Only by purely objective study can we know the characteristics of an organism, and having ascertained them with minute care we must, if necessary, make a new group in classification. The group to which the causal parasite of molluscum belongs I have named the Plassomyxineæ.

Scattered in cryptogamic botany are papers on species of *Synchytrium*, and in protozoology, accounts of Haplosporidia and Rhizomastigina; the parasite of molluscum has affinities with these and allied groups. They are all protists, and the related literature is part of protistology.

The unnatural divorce of cryptogamic botany from protozoology accounts for some of the delay there has been in recognising the molluscum body as a parasite.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

Meeting held on October 19th, 1922, Dr. H. G. Adamson, President of the Section, in the Chair.

(*Continued from p. 405, vol. xxxiv.*)

Dr. Hugh S. Stannus showed a case of (?) *pellagra*. The case now shown was one which, if it had occurred in an endemic area, would have been diagnosed without doubt as one of early pellagra. He was anxious to elicit the opinion of the members of this Section as to whether the lesions presented could be explained on any other pathogeny. The man was chief storekeeper to the Nigerian Railways, and went to West Africa some fifteen months ago for the first time. Three or four months after his arrival he developed an acute dermatitis, involving the exposed portions of his hands and wrists and neck and lower part of the face. Bullæ formed, and later scaling took place. The areas involved were strictly those exposed to sunlight according to his dress and head covering. He showed other slight but suggestive symptoms: there was some disturbance of the epithelial covering of the tongue, with a resulting leucoplakia-like condition in some areas and in others some slight denudation; there was also some heaping up of white sodden epithelium at the muco-cutaneous junctions at the angles of the lips, and some discoloration at the external canthi—signs to which a good deal of importance was attached. He had suffered from dyspepsia and constipation, and became rather depressed about the persisting condition of his hands, but had no frank nervous symptoms. Before going to Africa he had never been out of Europe. He stated that he had always had a skin sensitive to sunburn.

Dr. Pernet said he had seen pellagra in Italy and one or two cases in London, and this case did not somehow seem to fit in with that diagnosis, but might be due to sun exposure in West Africa.

Dr. Whitfield said that although he had seen a number of cases of solar disturbance of the skin in Colonials, the condition was not like that of this patient; there was none of the smudgy pigmentation with hyperkeratosis at the back of the hands which were seen in solar cases. What struck him as characteristic of pellagra was the extremely defined edge, which was never seen in Colonial cases of sun disturbance. The patient had a very smooth skin, with a definite edge, and a little line of pigment beyond.

Dr. H. G. Adamson (President) said that the so-called solar skin only

developed after years of exposure: it was not an immediate effect of strong sunlight. On the fingers the condition looked like lupus erythematous.

Dr. STANNUS (in reply) said the descriptions of pellagra in the text-books were often very misleading: they appeared to have been copied from one book to another, and were mostly descriptions of full-blown cases of many years' standing. The features of the present case were all characteristic, and he agreed that the condition known as "sailor's skin" was only produced after many years: if there were no other hypothesis offered in explanation, he believed it to be a case of pellagra. As regards the sensitiveness to sun-burn, he believed it was no more than was commonly seen among individuals of the same degree of fairness.

Dr. A. WHITFIELD showed *photographs of demodex impetigo.* A few meetings ago he showed photographs of a case of impetigo of bullous nature, in which he discovered the demodex, and he found the condition had been described in Australia. Since then he had had a considerable number of cases. All his earlier cases were at the age of puberty, or later, *i. e.* at an age when demodex might be found in the skin. Therefore he had been on the look-out for a much earlier stage. Recently a child, aged 15 months, was brought to his out-patient department with an extraordinary bullous impetigo, and he said it would be worth while to look for the demodex in it, and it was found. Demodex had not been described on the skin at 15 months of age, and at that age, unless camphorated oil had been rubbed in, the children had no comedones. This case therefore was evidence that there was a definite association between the demodex and impetigo in some instances. The fact that he was now able to prophesy the cases in which one was likely to find the demodex appeared to him to be evidence that it had some causal relationship in the production of the disease or in the development of special features.

Dr. HALDIN DAVIS showed a case of *sclerodermia.* The patient, a woman, aged 56 years, presented a condition of the skin which he had called sclerodermia, although it was not quite like an ordinary case of that disease. The whole skin of the trunk, extending from the clavicles to the tops of the thighs, was unnaturally smooth and of the consistency of hard wax. It remined one of a case of sclerema neonatorum. The patient found that it made it very difficult for her to stoop owing to its stiffness. She also complained bitterly of the severe pruritus which it caused. The condition dated from about nine months ago, when she was wearing a ring pessary, which she

neglected to change for several months. It appears probable that the cutaneous disorder had been caused by septic absorption due to the presence of this foreign body for too prolonged a period in the vagina. Other examples of sclerodermia due to septic absorption had been published, but as a rule due to septic teeth. These could not have been the cause in this patient, for she had had all her teeth extracted some years ago.

Dr. Graham Little regarded the case as diffuse sclerodermia. Septic absorption of diffuse sclerodermia was present in a case of his own, which he had shown before the Section. That patient had a large part of the body immobilised by sclerodermia, so that she could not feed herself, and she had to be carried up and down stairs. The condition was advancing. The whole of the affected areas cleared up astonishingly with the removal of all her teeth, many of which were septic. She was now earning her living by type-writing, the last thing of which one would have thought her physically capable.

Dr. G. Pernet said he considered this was a typical and characteristic case of sclerodermia. Many years ago he saw a similar condition in a middle-aged clergyman, whose abdomen and other parts of the trunk were completely sclerosed. In the patient now shown the appearances about the nipples were of interest, as those areas had escaped involvement.

Dr. Haldin Davis showed a case of *angiokeratoma*. The patient, a girl, aged 17 years, presented a very striking example of angiokeratoma on the hands. They first began to be affected about seven years ago and had become steadily worse year by year. There were numerous typical lesions on all the fingers of both hands, small bluish swellings deeply imbedded in the skin and surmounted by thin horny caps. All the digits were fat and puffy, the circulation was obviously very sluggish, and during the winter she suffered greatly from chilblains. The condition was a very serious handicap to her as it prevented her from doing any ordinary work.

Dr. F. Parkes Weber said that some years ago* he showed a case of severe angiokeratoma of the hands, in which the fingers and toes, on Röntgen-ray examination, showed bone-changes somewhat resembling those occurring in sclerodactylia. These bone-changes had since increased. He thought that the so-called angiokeratoma of the scrotum was to be separated decidedly from angiokeratoma of the hands.

Dr. H. G. Adamson (President) said that the classical case of this disease was the one Dr. Pringle described, with a coloured drawing,† almost exactly like this patient's hands. It was a characteristic affection, and occurred in people with a

* F. Parkes Weber, "Angiokeratoma, with Bony Changes," *Proc. Roy. Soc. Med.*, 1914, vii (Clin. Sec.), p. 25.

† *Brit. Journ. Derm.*, 1891, iii, pp. 237, 282, 309.

chilblain circulation. It was very common in Italy. There were dilated vessels, and they formed little cysts in the skin. The hyperkeratosis was a secondary condition over the top of the dilated vessels.

Dr. A. Eddowes said that two essential points should be kept in mind in the treatment. The first was to try to soften the warty collections of epithelium, and the second was to help the circulation artificially. It would be useful for this girl to wash her hands at night in warm water, and afterwards rub into them cold cream containing boric acid to remove the horny accumulations, and to wear gloves in cold weather. The hands should also be massaged.

Dr. J. H. Sequeira showed a case of *xanthoma diabeticorum*. Patient, a male, aged 25 years, was discharged from the army in 1919 with diabetes and had since been under Dr. Leyton, who had been treating him dietetically since 1921. He showed quite clearly small oval or rounded flat xanthoma lesions arranged in lines along the flexion creases of the hands. There were similar nodules arranged in groups over the knuckles and elbows and on the dorsum of the feet. The lesions had lessened since he had been dieting himself strictly. At the meeting of the Dermatological Association in London last year he showed a woman who had ten times the normal amount of cholesterin in the blood and who showed similar xanthoma lesions, but this man's blood, tested in the same laboratory, showed slightly less than the normal percentage of cholesterin in the blood.

CURRENT LITERATURE.

INFLAMMATIONS, ETC.

EARLY LESIONS AND THE DEVELOPMENT AND INCIDENCE OF LEPROSY IN THE CHILDREN OF LEPERS. L. Gomez, Basa and Nicolas. (*The Philippine Journal of Science*, September, 1922, xxi, No. 3, p. 233.)

Since 1906 the lepers in the Philippine Islands have been segregated on Culion Island. The colony established at present contains a population of about five thousand. Between 1906 and December 31st, 1921, 689 children were born in the colony. Of this number 333 died and 51 were sent away from Culion. Three of them returned later to the colony. At the end of 1921 there were 308 children who had been born in the colony both parents in the majority of cases having been lepers. These children born of leper parents and living among lepers offered favourable material for the study of the early lesions in the development of the disease.

The paper of Gomez, Basa and Nicolas is the result of the study of the records of the colony, and repeated clinical and bacteriological observations were made between June, 1921, and March, 1922.

These observations show that children born of leper parents showed the same susceptibility to other illnesses as children of non-leper parentage, but the mortality was higher on account of congenital debility. This mortality is counterbalanced to some extent by the lesser mortality from infantile beri-beri, which disease has practically disappeared in Culion with the exclusive use of unpolished rice in the dietary. The most frequent recognised site of the early lesions of leprosy is the skin. Infection through the integument is favoured by the great prevalence of skin diseases among children, these diseases offering conditions favourable to invasion of the lepra organism.

The most frequent early lesion recognised is macular, which in Filipino children is in the form of whitish fawn-coloured patches. In the early stages the bacillus may not be found in these lesions and sensory disturbance or alteration in the secretory power of the glands is not noticed. Later the nervous symptoms appear and heat discrimination is the first affected. The white patches are either precursors of other skin and nervous manifestations, or develop into progressive and bacteriologically positive leprous lesions, with anæsthesia and anhidrosis. In a few instances the leprous lesions disappear spontaneously. 7.79 per cent. of the 308 children of leper parents born and living at the time in Culion Island were positive lepers, and 25 per cent. had suspicious or definite signs of leprosy although the disease was not proved bacteriologically. The youngest found to be a positive leper was three years old, but suspicious lesions were found in children as young as a year.

The paper is of great interest, the cases are well worked out and there is an admirable series of photographs. J. H. S.

MANUFACTURE OF CERTAIN DRUGS FOR THE TREATMENT OF LEPROSY. G. A. Perkins. (*The Philippine Journal of Science*, July, 1922, xxi, No. 1, p. 1.)

The report refers to previous chemical investigation of leprosy by the Bureau of Science in the Philippines, the work having been placed in the hands of a committee. The Bureau of Science has prepared a number of drugs which have been used experimentally at San Lazaro Hospital and the Culion Leper Colony. The present paper is written from the chemist's standpoint and deals with their preparation and chemical composition.

Chaulmoogra oil is a fixed vegetable oil composed almost entirely of fatty acids combined with glycerin. The acids of Chaulmoogra are found nowhere else in nature and have not been synthesised in the laboratory.

The mixed ethyl esters of the fatty acids of Chaulmoogra oil have been on the market under the term "Antileprol." These substances appear to be more easily absorbed than the oil. They have been used intramuscularly and intravenously. Details are given of their manufacture.

Muir's E.C.C.O. has been used by the committee as well as sodium gynocardate A. & S., and also an emulsion of the oil.

Experiments have also been made with sodium morrhuate and also with cod-liver oil ethyl esters.

The experiments are still in progress, but it may be stated that the intramuscular ethyl ester treatment has been decided upon for the main routine treatment at Culion Leper Colony, and 40,000 doses per month are being manufactured for that purpose. J. H. S.

THE PRESENT STATUS OF LEPROSY IN THE HAWAIIAN ISLANDS. William Thomas Corlett. (*Arch. of Derm. and Syph.*, 1922, vi, p. 607.)

In this interesting paper the writer discusses the leprosy condition in the Hawaiian Islands, both with regard to the measures adopted for segregation and the treatment employed.

Complete segregation appears to be difficult to accomplish in the Islands, owing to the changes which take place in the policy of leprosy control consequent on the elective form of government. He found that leprosy was most prevalent during the school age, and was most common in the male sex. He considered that a specific for leprosy had not yet been found, and that though the more modern treatment with ethyl esters of chaulmoogra oil seemed to be of benefit in most cases, and especially in mild and early cases, in which it might arrest the progress of the disease for a time at least, the treatment was by no means certain, and in some cases appeared to aggravate the disease. He even went so far as to remark that "the enthusiasm with which treatment was received and entered into seems to have been in inverse ratio to the permanent benefit derived." Between July 9th, 1919, and March 31st, 1921, sixty patients were discharged from the leper settlement at Molokai. Of this number sixteen have since been returned to hospital, six have died while on parole, one is known to have escaped from the Islands, and only two have been released from parole as apparently cured, and these prior to the end of the four-year period (in which no symptoms of leprosy have appeared, the patient remaining during this time bacteriologically negative) now thought necessary. J. M. H. M.

HYPOSENSITIVITY OF THE SKIN COVERED BY A NÆVUS TELANGIECTATICUS IN A CASE OF ACUTE ECZEMA. L. Waelsch. (*Derm. Wochenschr.*, September 30th, 1922, lxxv, No. 39.)

A patient, aged 58 years, with a more or less generalised papulo-vesicular eczema, also exhibited a well-marked nævus flammeus in the region of the left scapula, axilla, and upper extremity, as far as the back of the left hand. The eczema, as expressed by papulo-vesicles, was sharply demarcated at the sinuous edges of the congenital stigma, but soon made its appearance on the islets of normal skin in its interior. It is well known that applications of adrenalin to such nævi leave the vessels uninfluenced: there is no local contraction—a lack of reaction explained by the absence of constrictor nerve-fibres in the vessels of such malformations.

Bereft of vaso-motor control, the tissues of a nævus should remain non-reactile to all forms of stimuli which do not actually destroy them. To test the theory, Prof. Waelsch applied a 50 per cent. solution of croton oil in olive oil to a vascular nævus in another patient, who consented to the experiment. It remained against the skin under zinc strapping on a cotton-wool swab for two periods of twenty-four hours without producing any inflammation of the nævus itself, although the adjoining normal skin showed active inflammatory changes in the follicles.

As the author points out, the experiment is open to the objection that in the one case an unknown stimulus had produced a frank or spontaneous eczema, and in the other there was dermatitis of known ætiology. H. S.

A PRELIMINARY STUDY OF THE EXPERIMENTAL ASPECTS OF IODIDE AND BROMIDE EXANTHEMS. Udo J. Wile, Carroll S. Wright and Ned R. Smith. (*Arch. of Derm. and Syph.*, 1922, vi, p. 529.)

As a result of their observations, the writers come to the following conclusions: (1) That the pustules of iodide and bromide acne are not sterile, but that the bacteria present are probably due to secondary contamination; (2) that iodide and bromide are not found in the purulent material from the acneiform lesions; (3) that percutaneous sensitisation tests for iodide and bromide are uniformly negative, and cannot, therefore, be used to indicate ingestion susceptibility; (4) and that the local phenomena of iododerma and bromoderma are not explicable on simple bacterial or chemical grounds, but are probably explained as due to a complex biochemical reaction. J. M. H. M.

DRUG ERUPTIONS FROM THE CLINICAL ASPECT. Fred Wise and H. J. Parkhurst. (*Arch. of Derm. and Syph.*, 1922, vi, p. 542.)

After discussing the drug eruptions from the new arsenical preparations of the arsphenamin series, which are now familiar, the writer goes on to refer to the eruptions provoked by more recent synthetic drugs, which may be erythematous, urticarial, morbilliform, scarlatiniform, erysipelatous, bullous or erosive.

The drugs referred to are: Barbital and medinal (sodium salts of diethylbarbituric acid and diethylbarbituric acid); codeonal (codein-barbital); adalin and bromural (bromidethylacetylcarbamid and monobromisovalerylurea); phenobarbital (phenylethylbarbituric acid); cinchophen (phenylquinolincarboxylic acid); pyramidon (dimethylaminoantipyrin); melubrin (sodium salt of antipyrinamidomethansulfonic acid); acetylsalicylic acid; hexamethylenamin and phenolphthalein. J. M. H. M.

PROCAIN DERMATITIS AMONG DENTISTS. Henry Kennedy Gaskill. (*Arch. of Derm. and Syph.*, 1922, vi, p. 576.)

Procain is capable of producing dermatitis in susceptible people, and occasional cases of dermatitis of the hands occur in dentists from its use. The dermatitis which results from it is either of the papulo-vesicular type, or consists of a thickened verrucous condition of the ends of the fingers, with involvement of the nail-bed and hypertrophy of the nail itself. J. M. H. M.

EXPERIMENTS ON THE VARIABILITY IN SUSCEPTIBILITY TO POISON IVY. E. D. Brown. (*Arch. of Derm. and Syph.*, 1922, v, p. 714.)

The method employed was to place a piece of the fresh leaf of poison ivy, about 1 cm. square, on the left arm and hold it in place by a piece of adhesive plaster. At the end of 12 hours it was removed and a note was made when the erythema began. The susceptibility was judged by the time required to produce a reaction and by the different degrees of severity. Twenty students were tested in this manner, and the results obtained from them, together with observations on about 100 cases accidentally produced, led to the following conclusions:

(1) There is a variability in susceptibility in different persons and at different times in the same person.

(2) The time required for the onset of symptoms in 19 clinical cases in which reliable data were obtained was from 5 hours to 8 days.

(3) The eruption was spread over the body without conveyance of the poison from the initial lesions through the agency of the hand or clothing.

(4) The serous exudate flowing from the vesicles plays no part in spreading the eruption to other parts of the body.

(5) It is more probable that the poison is conveyed through the air by insects than by dust or pollen. J. M. H. M.

SYPHILIS.

THE WELANDER-HOME INSTITUTION. K. Grön and Joh. Haavaldsen. (Published by the Norwegian Oddfellow Lodge, 1922.)

This brochure gives an interesting account of the inauguration of the Welander Homes for congenitally syphilitic children in the Scandinavian countries and in Germany. The report of the Norwegian Vesle Home (Kristiania) shows the work of the ten years 1912–22 since its foundation. During this period 83 children had been admitted, of whom 53 had been discharged. As a rule no child was admitted under the age of 12 months. Of these 83 children 71 (*ca.* 85 per cent.) were illegitimate. Specific treatment was carried out, when required, at the Ullevaal Hospital, the home being maintained purely for the purpose of after-care and observation. W. J. O.

THE "TRÉPOL" TREATMENT OF SYPHILIS. Lehner and Radnal. (*Derm. Wochenschr.*, October, 1922, lxxv, No. 42.)

In a short but useful summary of 13 cases of syphilis in various stages treated by 10–12 injections each, on alternate days, of the 10 per cent. oily suspension of sod. pot. bismuth tartrate (trépol) in 2 c.c. doses, intramuscularly, the authors record their opinion that the treatment is valuable, especially in such cases as are refractile or intolerant of the Hg.-salvarsan combination.

The results on W.R. are herewith reproduced in tabular form.

Case number.	Symptoms.	The W.R.		
		On admission.	Directly after a course.	4–6 weeks after completion of the course.
1	Recurrence of secondary symptoms	+++	+++	+
2	Secondary symptoms	+++	+++	Negative
3	Primary chancre	+	+	,,
4	Secondary symptoms	+++	+++	,,
5	Tertiary symptoms	+++	+++	+
6	Primary chancre	Negative	Negative	Negative
7	Secondary symptoms	+++	+++	Failed to attend
8	Chancre	+	Negative	Negative
9	,,	Negative	,,	,,
10	Secondary symptoms	+++	+	,,
12	Chancre	Negative	Negative	,,

N.B.—In Case 11 (primary and secondary manifestations) and W.R. +++ the patient had a sharp rigor and vomited 3 hours after the second injection. The course was abandoned.

The 13th patient is being treated at the time of publication with visible improvement of buccal and lingual plaques (? leucoplakia), which had previously resisted energetic Hg. + neosalvarsan injections (neosalvarsan, 5 of 0·3 grm.; ditto, 6 of 0·45 grm.; Hg. succinimide, 10 of 0·03 grm.; Hg., calomel, 1 of 10 per cent.).

According to this paper the action of trépol on cutaneous and mucous lesions is exceedingly rapid and complete, and the infiltration of a primary chancre has usually disappeared by the fifth injection.

Constitutional symptoms (headache, etc.) clear up after one injection, and secondary lesions on the skin are found to involute after 3–4 injections, with the formation of pigment deposits.

[In only one of the 13 cases discussed was there any constitutional or severe local reaction to the drug, and in this one (Case 11) it would seem that the Herxheimer phenomenon might afford a satisfactory explanation.—Translator.] H. S.

LICHEN TREATED BY NEOSALVARSAN. Hodera and Behdjet. (*Derm. Wochenschr.*, August 26th, 1922, lxxv, No. 34.)

The favourable influence of arsenic in some cases of lichen planus needs no emphasis, and the authors in their short article only claim a greatly accelerated action of the drug when given in this form.

Their first case was a woman, aged 52 years, who had suffered from a typical papular lichen planus for six months. The lesions were situated on the dorsa of the hands, the forearms, legs, thighs and buttocks, and while in the main they were of the flat polygonal type, there were also a considerable number of conical papules round the hair-follicles. Great itching was associated with all of them. Following the observations of Prof. Dind (Lausanne), who incidentally regards the so-called neurodermite, or lichen "Vidal," as identical with lichen planus, five intravenous injections of neosalvarsan in rising dosage, 15, ·3, ·45, ·6 and ·75 grm. at intervals of 4–5 days in the first three, and 8–10 days for the last two injections were given. Within a fortnight of the last injection all the lesions had been absorbed, and were pigmented—a cure in six weeks, which by oral administration of arsenic would scarcely have been obtained in four months.

Two other cases were treated similarly, and with equal success. In the third case the authors diagnosed typical neurodermatitis of a year's duration. Considering the intractability of this affection and the lack of response even to X-rays in some cases, this addition to the therapeutic armamentarium would be valuable. H. S.

A LICHEN PLANUS ERUPTION AFTER ARSPHENAMIN. Lawrence K. McCafferty. (*Arch. of Derm. and Syph.*, 1922, vi, p. 591.)

In the case here reported, a mulatto woman, suffering from syphilis, developed after nine intravenous injections of arsphenamin a lichenoid eruption on the trunk and arms, which closely simulated, both clinically and histologically, lichen planus. The eruption was associated with symptoms of arsenical poisoning, and on this account it was believed that the arsphenamin was the cause of it, and that it was not a coincidence. Cases of arsenical dermatitis assimilating lichen planus have been described previously, but in no case reported has the appearance been so similar to that disease. J. M. H. M.

DR. J. J. PRINGLE.

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OBITUARY.

JOHN JAMES PRINGLE, M.B., C.M.Edin., F.R.C.P.Lond.,
Consulting Physician, Skin-Department, Middlesex Hospital.

By the death of Dr. J. J. Pringle Dermatology suffers a very great loss. During nearly forty years he worked devotedly for the advancement of the knowledge of diseases of the skin, and particularly in the cause of British Dermatology. Although he wrote no text-book and contributed comparatively little to the literature of skin-diseases, he was well known and highly regarded for his learning and skill, not only in this country but on the continent and in America.

He was ever alive to all that was new in work or ideas in the dermatological world, and helped by his ardour and encouragement to stimulate the interest of others. Several of his former pupils now in charge of dermatological departments in teaching hospitals in London owe much to his impellent and kindly influence as well as to his example and teaching in their earlier years.

Dr. Pringle graduated in Edinburgh in 1876, at the age of twenty-one, and after holding the post of House-Physician at the Royal Infirmary he spent some years in Paris and Vienna, when his interest in skin-diseases was already apparent, since he attended the clinics of Vidal and Fournier, of Hebra and Kaposi.

He became connected with the Middlesex Hospital in 1882 and held the post of Medical Registrar from 1883 to 1885. Then for ten

years, from 1885 to 1895, he was an Assistant Physician, and from 1892 to 1895 Lecturer on Practical Medicine, thus laying a sound foundation in general medicine for his subsequent work as a dermatologist.

In 1885 we find him an active member of the Dermatological Society of London, which had been founded three years before and of which he was Secretary for the next sixteen years.

From 1888 until his retirement thirty-two years later, in 1920, he was Physician for Diseases of the Skin at the Middlesex Hospital, following Dr. Robert Liveing, to whom he had been previously assistant.

From January, 1891, to December, 1895, as Acting Editor of the *British Journal of Dermatology*, he so ably fostered through its early childhood that offspring of the Dermatological Society which Malcolm Morris had nursed in its infancy.

In 1895 he relinquished the editorship of the Journal to take up his work in connection with the Third International Congress of Dermatology to be held in London in 1896, a work which found him at his very best. His fluency in foreign languages, his personal acquaintance with many continental dermatologists, his facility and graciousness in correspondence and his instinct for organisation all helped to make of this one of the most successful congresses that has been held; and he was always justifiably proud of the "volume of transactions" which remains as a monument of his energy and enthusiasm. His foreign colleagues conferred upon him the honour of Corresponding Member of the Dermatological Societies of France, Vienna, Berlin, Italy and Lisbon.

From 1913–1915, as President of the Dermatological Section of the Royal Society of Medicine, the genial influence of his charming and sprightly personality and his keen interest in the work of the Section suffused and enlivened every meeting; during his term of office he instituted special discussions on three important subjects, namely, pityriasis rosea, mycosis fungoides and pemphigoid eruptions, introduced respectively by Dr. Graham Little, Dr. Sequeira, and Dr. MacLeod.

During the war, already now past his sixtieth year, and in indifferent health which often confined him to his bed, he carried on his work at the hospital, and took control of the Department for Diseases of the

Skin at the No. 3 London General Hospital at Wandsworth, together with a large military out-patient clinic at Millbank. Later on he organised at his own hospital the Department for Treatment of Venereal Diseases and continued his work in this and in the Skin Department up to the age limit of 65 years. To the end of 1922 until a few weeks before he left London for a voyage to New Zealand, he attended our meetings and took an active part in committee work with a courage and spirit which was the admiration of his friends, and which quite hid from strangers the fact that he was seriously ill. He died in Christ Church, New Zealand, on December 18th.

Of Pringle's personal characteristics it may be said that he was accurate, precise and punctilious in everything—a preciseness which was relieved by his sense of humour, and embellished and made very attractive by his fondness for the ornate. These characters of neatness with ornament were seen in his speech, in his writing, in his dress, and in his household surroundings. He had, too, a liking for colour, akin to his great love of music.

A very pleasing trait was that he gave the same care and attention to detail and extended the same kindness and courtesy to his hospital patients, whom he would address as "My dear madam" or "My good fellow"; and he would sometimes visit at their own homes the poorest of his patients who were too ill to attend at the hospital, seemingly in so striking contrast with his dapper dress and appearance.

Many both in and out of the profession and in all stations of life lose a very loyal friend. As has been said by one of his old pupils, "no one will ever know half of his kindly acts and generous deeds."

Although it has been said that Dr. Pringle wrote comparatively little, he made very careful notes on cases in which he was particularly interested. Some of these were published as papers in the *British Journal of Dermatology*, and in two or three instances were the first descriptions of the disease to be published in this country, so that Pringle's name afterwards came to be associated with these complaints, viz. Adenoma sebaceum, angiokeratoma and "Pringle's seborrhoïde." A few other cases were so fully recorded in the *Transactions of the Royal Society of Medicine* that they must be included in a list of his publications:

(1) "A Case of Adenoma Sebaceum" (coloured plate), *Brit. Journ. Derm.*, vol. ii, 1890.

(2) "On Angiokeratoma" (illustrated), *ibid.*, vol. iii, 1891.

(3) "Tubercular Lymphangitis," by John Cahill, with remarks by J. J. Pringle, *ibid.*, vol. vii, 1895.

(4) "Actinomycosis" (coloured plate), *Med.-Chir. Trans.*, vol. lxxviii, 1895.

(5) "A Case of Peculiar Multiple Sebaceous Cysts" (Steatocystoma Multiplex), *Brit. Journ. Derm.*, vol. xi, 1889.

(6) "Multiple Epitheliomata on Lupus Erythematosus," *ibid.*, vol. xii, 1900.

(7) "A Rare Seborrhoïde of the Face," *ibid.*, vol. xv, 1903.

Some cases published in detail in the *Transactions of the Dermatological Section of the Royal Society of Medicine*:

(1) "Mycosis fungoides," *Brit. Journ. Derm.*, vol. xxv, 1913, p. 415.

(2) "Four Cases of Angiokeratoma in one Family," *ibid.*, vol. xxv, 1913, p. 40.

(3) "Extensive Carcinoma of the Face occurring in Xerodermia pigmentosa treated by Radium" (illustrated), *ibid.*, vol. xxvi, 1914, pp. 144–150; *ibid.*, vol. xxviii, 1916, p. 253.

(4) "Mycosis fungoides à tumeurs d'emblée" (illustrated), *ibid.*, vol. xxvi, 1914, pp. 150–153.

(5) "Pemphigus vegetans," *ibid.*, vol. xxvii, 1915, pp. 63–66, pp. 233.

(6) "Miscalled Multiple Idiopathic Hæmorrhagic Sarcoma of Kaposi" (illustrated), with report of pathological sub-committee, *ibid.*, vol. xxx, 1918, p. 179, vol. xxxi, 1919, pp. 143–150.

Articles on Skin Diseases, *Fowler's Dictionary of Practical Medicine*, 1890.

Articles in *Quain's Dictionary of Medicine*, 1901, on Eczema, Depilatories, Mycosis fungoides, etc.

Articles in Clifford Albutt's *System of Medicine*, 1911: Ichthyosis, Affections of the Pigmentary System, of the Sweat Glands, of the Sebaceous Glands, Angiokeratoma, Darier's Disease.

Editor of the English edition of *Jacobi's Portfolio of Dermochromes*, and of the *Pictorial Atlas of Skin Diseases* (*St. Louis Atlas*).

H. G. Adamson.

The small community of London dermatologists has lost one of its most notable personalities in the death of John James Pringle, which occurred in New Zealand on December 18th, while he was on a voyage in search of health. "J. J.," as he was affectionately dubbed by his friends, was the third son of Andrew Pringle, of Borgue, Kirkcudbrightshire, and claimed descent from the famous John Pringle, author of *Observations of Diseases of the Army in Camp and Garrison*, published in 1752. "J.J." took his degree of M.B., C.M., at Edinburgh in 1876, and with characteristic *insouciance* never tried for the higher degree, but went abroad to study dermatology in Paris, where he spent the best part of two years, Vienna, and Berlin. It is very typical of the man he was that he acquired an extraordinary command of the French language by nightly attendance at performances at the Comédie Française for a full six months. Frenchmen have told me that his accent and ease in speaking French were so perfect that few would believe that he was not actually French, and indeed in Berlin he was known, sometimes to his discomfiture, as "the Frenchman." He always loved the French and had many warm friends of that nation. They in turn loved and appreciated his gaiety and wit, and especially that most consistent and lifelong characteristic, his sense and practice of immaculate dress. "Ce Cher Pringle, toujours tiré à quatre épingles," was a rhyme coined by the contingent of French dermatologists whom he invited to attend the Dermatological Section of the British Medical Association, over which he presided with characteristic *bonhomie* and *éclat* (French locutions seem inevitably required to describe Pringle) at Cheltenham in 1901. Pringle's life work was done at the Middlesex Hospital, where he became Assistant Dermatologist, with Robert Liveing as his chief, and on Liveing's retirement had full charge of that department until his own retirement under the operation of the age limit of 65, some two years ago. During his tenure of this post he trained at least five assistants who came themselves to be heads of dermatological departments at hospital schools in London. He took the keenest interest in teaching and diagnosis up to the last, and although he never undertook the writing of a formal text-book, which no doubt would have bored him horribly, he contributed innumerable articles to the *British Journal of Dermatology*, which he helped to found, and to other medical publications, contributions which in their sum and their authority

constitute a very respectable body of achievement. Those of us who are senior enough to have belonged to the old Dermatological Society of London, which came to an end fifteen years ago, best remember Pringle, then in his prime, and in the fullest flowering of his whimsical personality, at meetings of that Society, to which he acted for very many years as Secretary, and his unrivalled flair in diagnosis was a valued asset of that Society. Dull men affected to look down on Pringle as a mere *dilettante*, for he had many interests and aptitudes outside his profession, especially in music, painting, and the "art of living." But the solidity of his judgment and knowledge of his chosen speciality, gained apparently without effort, often irritated, while it confuted, these narrow and envious critics. Never were these qualities better exemplified than during his tenure of the Presidency of the Dermatological Section of the Royal Society of Medicine in the eventful years 1913–1915. In the opinion of many he was much the best President the Section has ever had. Pringle never suffered fools gladly, and his caustic quashing of tiresome speakers is a hilarious memory with those of us who did not feel his lash. He took the duties of the office very seriously. By his request the manuscript of the contributions sent for publication was submitted to him for revision, and having himself a sensitive sense of style, he was wont to use the blue pencil very freely, or would even write, when correction seemed too hopeless, to the offending member, requesting a recasting of the contribution *ab initio*.

One afternoon in the summer of 1903 Pringle dropped unconscious on the pavement in front of a chemist's shop in London, suffocated by a pulmonary hæmorrhage, of which he nearly died. This was the first intimation of the fell disease which from that date was to mar his activities and darken his life. Six months at a sanatorium 1903–1904 seemed to restore him completely, and few but his intimates knew what an unceasing struggle, faced with an invincible courage and cheerfulness, he maintained against an ever-advancing invasion of one organ of the body after another by tubercle. It is sad that he should have met his end so far from his many friends, in whose lives his death leaves a blank not to be filled.

E. G. Graham Little.

TREATMENT OF CHRONIC ECZEMA WITH CONCENTRATED CARBON ARC LIGHT (FINSEN).

SVEND LOMHOLT, O.B.E., M.D.

From the Finsen Institute, Copenhagen (Director: Dr. A. Reyn).

During the last few years X-rays have been used in an increasing degree in the treatment of chronic eczema. Actually they have proved to be most useful in many cases of this disease and especially in old infiltrated chronic cases. Often a few applications suffice to remove an old much-infiltrated patch. X-ray treatment, however, cannot be looked upon as an ideal treatment for chronic eczema. In some cases it may fail, completely or partially, and it does not prevent relapses.

With regard to this important point two facts must be remembered. Firstly, X-ray treatment always has certain dangers. Not to mention the risk of a technical mistake, which may cause a severe burn, we sometimes meet with secondary atrophy of the skin with an accompanying disfiguring dilatation of the superficial blood-vessels or even with delayed ulceration. Moreover, an atrophy can be produced by a quantity of X-rays which does not give any visible acute reaction (erythema) of the skin when the treatment is repeated a sufficient number of times. Often the first visible manifestation of an atrophy appears years after the last treatment was given. Secondly, we must remember that the result of repeated X-ray treatment will generally prove to be inferior to that of the first treatment, and the number of failures will rapidly increase in proportion to the number of repetitions. We meet with a certain number of cases of chronic eczema growing more and more intractable to X-ray treatment. Unfortunately also such cases will at the same time grow correspondingly intractable to all other ordinary remedies. In many cases the first result will be a dermatosis, which is completely untouched by any remedy at all. Probably this undesirable effect of X-ray treatment is due to the damaging effect of the rays on the tissue cells; the vitality and the self-regenerating power of the structures of the skin are diminished,

as can be seen very clearly by the fact that all the hairs and all the sweat-glands disappear from the atrophic area of skin.

In the Finsen Institute at Copenhagen the application of concentrated light from a carbon arc lamp (as recommended by Prof. Finsen* for the treatment of lupus vulgaris) has in many cases proved itself capable of considerably improving these resistant cases. The Finsen-light treatment possesses an extraordinary but obvious power of stimulating the vitality of the skin, producing a remarkable and durable hyperæmia in the tissue. This power of the light was demonstrated by Prof. Finsen himself and afterwards studied in a detailed way by many of his assistants, especially by Dr. H. Jansen in a large number of histological researches.

The observation of this good effect of the arc light on the atrophy of a skin area injured by X-ray treatment encouraged us to see whether a corresponding effect might not be obtained by treating chronic eczema with this kind of light from the very beginning. Therefore during the last year a considerable number of experiments were made in treating some chronic and apparently intractable cases of eczema by Finsen light. I want at once, however, to point out that the exposure to the light was considerably diminished in these experiments as compared to the ordinary exposures used in the treatment of lupus. In this treatment the ordinary single exposure for each spot to be treated was 70–140 minutes daily of a carbon arc light of 50 ampères and 55 volts. In the eczema treatment the ordinary exposure is but 15 to 20 minutes, though in exceptional cases only increased up to 30 or even 60 minutes. For obvious reasons the exposure must be varied in proportion to the thickness of the skin in question. Often the original thickness has been increased by the development of keratotic tissue in the epidermis of the eczema patch. The reaction produced by this amount of light will be somewhat similar to that of a burn of the first degree. Still, it differs absolutely from a simple burn. It appears slowly, it affects the skin much more deeply, though it produces but a slight destruction of the tissue as compared with that of a burn.

The results were almost amazing. The first case treated was a blacksmith who had been suffering almost continuously for 35 years

* Finsen, *Phototherapy*, London, 1901 (Arnold); A. Reyn, *Die Finsentherapie* (Meusser: Berlin, 1913).

from a bad eczema on the back of both hands, with much infiltration, scaling, and, in many places, minute vesicles. He had been treated in the Institute for about 15 years but only with poor results. X-rays had altogether been applied 28 times, but still extensive relapses occurred. He was then treated with concentrated carbon arc light. The quantity of light given was one hour to each spot, and this treatment was repeated three times. After the reaction had disappeared the skin was completely healed and rapidly became almost normal. Despite the fact that he immediately took up his hard and dirty work, the skin of his hands remained smooth and sound and has now remained so for more than a year.

This fine and rather unexpected result inaugurated a long series of new experiments on the same lines. Nearly a hundred patients with chronic eczema have now been treated with this local concentrated carbon arc light, including all sorts of chronic eczema, viz. infiltrated and dry ones, vesicular and scaling ones, and especially many inveterate and keratotic cases. The result was that about 60 per cent. were completely cured. All subjective symptoms (itching, etc.) disappeared, and at the same time the objective symptoms decreased to a minimum. A slight infiltration only remained in some of the cases, such as might be expected in a skin, that had been submitted to pathological alterations for a long time, sometimes for several years. Of the remaining 40 per cent., about 25 per cent. were more or less improved, and in 15 per cent. only the result was but transitory, if not completely negative. It is of great importance to state the fact that no single one of all these cases was aggravated. This means a most evident advantage in comparison with the X-ray treatment.

The eczema cases most suitable for light treatment are without doubt the old dry infiltrated and keratotic ones—those which are generally characterised by the name "neurodermitis chronica" or "lichen chronicus (Vidal)." In addition many vesicular cases were favourably influenced by this treatment. It would not be of much use to give the history of all these cases, most of them being very much alike. I shall therefore limit myself to a few typical histories which will illustrate the results obtained in a clear way. I regret very much that illustration by photographs proved to be rather disappointing, owing to the fact that the original pathological alteration of the skin

in eczema patches does not give such obvious impressions to the photographic plate as to differ distinctly from those given by the pigmentation and other residua left in the place of the patches after they have been cured.

Case 1.—Male, aged 54 years (mentioned above).

Case 2.—Male, aged 63 years. For many years large patches of much infiltrated, itching, chronic eczema (neurodermitis) on both legs (10 × 15 cm.), and on both arms (5 × 10 cm.). Treated with many different ointments, etc., without any obvious result. Was submitted to four treatments of 15 minutes with carbon arc light from December 13th, 1921, to February 15th, 1922. May 2nd, 1922, the lesions are cured. No itching in the patches. The skin remains smooth, pliable, with a slight infiltration only.

Case 3.—Male, aged 10 years. For four years a chronic eczema patch (5 × 5 cm.) of the "neurodermitis" type in the left popliteal space. Treated with many different ointments and with X-rays several times without permanent result. February 9th to March 27th, 1922, three treatments of 15 minutes. May 2nd, 1922, the skin remains completely smooth. August 30th, 1922, a small relapse in the left popliteal space. Treatment of 15 minutes. September 25th, 1922, the skin is now again quite natural.

Case 4.—Male, aged 56 years, a waiter. For six years a large infiltrated scaling patch on the back of the right hand and another much infiltrated patch on the right leg. December 6th and December 15th, 1921, treatment of 15 minutes. January 5th, 1922, completely cured.

Case 5.—Female, aged 25 years. For 6 years permanent eczematous lesions in both hands, treated in vain with large doses of X-rays. At present many infiltrated keratotic, fissured eczema patches, especially on the fingers of the right hand. May 6th and 13th, 1922, treatment of 15 minutes. June 28th, 1922, the skin remains completely cured. September 7th, 1922, no sign of a relapse.

Case 6.—Male, aged 63 years. Has been suffering from a "lichen ruber" for about fourteen years, which had left some very extensive and infiltrated patches on all the four limbs. The largest of the patches measured 10 × 15 cm. A severe permanent itching accompanied the disease. May 17th and June 21st, 1922, light treatment of 15 minutes. The result was good. The skin grew almost completely smooth and natural, and also the intense itching disappeared completely. In the following six months no relapse had yet occurred.

As mentioned before, the ordinary time given in a single exposure was 15 minutes, but it was often increased, especially if this dose did not produce the desired reaction on the skin. The amount of light to be given depends amongst other things on the size of the skin area in question and on the infiltration of the patch. A patch placed directly over a bone, *i.e.* on the surface of the tibia, does not need as much light as a patch on the back of the leg.

The results obtained were very encouraging, especially in a certain number of old refractory and torpid cases. The majority of these

were completely cured by a single or a few treatments. Still, we must remember that the Finsen treatment is a somewhat laborious and expensive treatment, therefore it should not be recommended as the treatment of all cases of eczema. It must be limited chiefly to such cases as remain uninfluenced by our ordinary methods of treatment. In such cases, however, it has proved to be of great value. The arc light treatment should also be chosen rather than X-ray treatment in cases where the latter does not give a definite result after the first treatment. To repeat the X-ray treatment over and over again means a serious risk of injuring the skin permanently. Here the Finsen light treatment ought to be preferred, and certainly it is often a most excellent help. As to relapses, not even the Finsen treatment can definitely prevent these. It has, however, a certain stimulating effect upon the nutrition of the skin, by the production of a better local blood supply, and thereby the skin is made more resistent to relapses. In cases where relapses do occur they are seldom localised to the original position of the patch, but chiefly to areas that have not been previously treated with light. Moreover, the light treatment can be repeated over and over again without causing any damage to the skin, and it combines well with all the other well-known local remedies for eczema.

A WASSERMANN MICRO-TECHNIQUE NEEDING ONLY OCCASIONAL TITRATION OF THE COMPLEMENT.

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The important conditions implied in the title—almost halving the work of the routine Wassermann test—are fulfilled by taking the complement harmlessly at intervals from healthy well-kept male cavies whose individual complement titre has been repeatedly tested at intervals and always found suitably constant. The testing ought to be, firstly, without antigen and with antigen by the well-known method of McIntosh and Fildes, and secondly, in each of these conditions in turn together with each of various control sera in turn. The "secondly" testing may of course be done along with the routine diagnostic tests. And indeed when once the cavy's titre has been reasonably settled, the "firstly" testing, if considered still necessary, may for time-saving be done at the same time as the routine actual test.

Although a small percentage of male cavies have by competent observers been found to show from time to time slight variations in the quality of their individual complements, yet in the few healthy well-kept male cavies that I have been able to test repeatedly during the last two years such *variations* of individual complement have not been detected by the routine titrations carried out. (But of course individual *differences* among the various cavy-sera have been appreciably constant.)

The importance of such complement constancy lies not merely in its saving about ninety minutes of the ordinary test-time, but also in its otherwise contributing to the standardisation of the Wassermann test. For as Scott and Griffith* state—"Of all the reagents in the Wassermann reaction complement is the least capable of standardisation, and

* Scott and Griffith, *The Complement Fixation Test in Syphilis*, p. 21. London: The Ministry of Health, 1920.

it is certainly the reagent which is most often responsible for discrepancies in the results on different occasions." To kill the cavy that has yielded as it were the golden egg of known excellent complement is not wise if, as seems by this micro-technique, such killing is avoidable.

Moreover, even if such complement-constancy is not universal in healthy male cavies, nevertheless constant individuals may be selected and, with also selected females, may, I hope, even be bred selectively—as I suggested to the Medical Research Council in forwarding in 1918 my results of the criterion tests mentioned below.

I make the present interim report hoping that the useful test-abbreviation will be further worked out by me, and also by others provided with larger facilities.

The micro-technique that I have found to succeed with the available small quantities of constant cavy-serum was devised in 1912, as a one-tenth-scale transposition of the well-known method of McIntosh and Fildes, and was mentioned by me in the *Lancet*, 1912, i, 1752, as having been used in a comparison of Wassermann methods. A rough outline of the micro-technique was given in the *Lancet*, 1916, ii, pp. 423 to 429. There I mentioned that I had used my technique in a comparative test of the small remainders of 263 sera and c.s.fs. with four different antigens just after the same samples had been tested by Dr. Fildes, and that in the test the micro-technique agreed with the macro-technique in every case even quantitatively.

Then in the M.R.C.'s comparative test of the 104 criterion sera of assorted cases investigated clinically in the London Hospital by Dr. J. H. Sequeira, I had the honour to be one of the "four pathologists who submitted their work to this open test." (See M.R.C. Special Report, No. 21, 1918, *The Diagnostic Value of the Wassermann Test*, p. 4). In this important series of tests, lasting for three months, the micro-method came out in the qualitative returns apparently without an error, and, as far as in the roughly quantitative returns it differed from the macro-methods, it was, as can be seen by scanning the Tabular Summary of the Results (*op. cit.*, pp. 50–53), in no case at a disadvantage.

These successful results in severe tests are, I think, due in the first place to the correctness of the macro-technique of which the micro-

technique is a transposition, and in the second place to the precision, largely automatic, of the drop-measuring method, and to such entire freedom from the distraction of washing pipettes during the test as is secured by the use of a sufficient assortment of simply gauged pipettes, rather than to any great skill from practice of the method. Indeed for four or five years before I undertook the weekly tests of the M.R.C. sera, other very varied work had not left me free to touch Wassermann work.

During the last couple of busy years at this children's hospital I have found the technique very suitable for the routine batches of up to 30 or so sera, especially with such improvements as I have been able to introduce into it.

Now Dreyer and Ward's standardised modification of the flocculation test promises an improved further valuable means to the diagnosis of syphilis. But, as described in the *Lancet*, 1921, i, p. 956, the flocculation method would seem to have the disadvantage that it statedly requires 4 to 5 c.c. of sterile blood taken by venepuncture.

In infants, however, the superior longitudinal sinus is the only accessible vein of suitable size. And infants requiring a test for syphilis are usually feeble and marasmic. So, even if the withdrawal of the 4 or 5 c.c. required were not somewhat against the child's feeble chances, there might seem to be some danger of determining more frequent thrombosis of the superior longitudinal sinus—a not uncommon cause of death in infant autopsies.

But from such little patients the small amount of blood required for a micro-Wassermann test can, without venepuncture, be obtained, even sterile, without difficulty, danger or even upset, especially by the simple procedure described below. The testing of such infants is facilitated by a simultaneous test of the mother, especially in the case where both turn out negative. (It is worth while to reassure the mother by taking her sample first.) But not infrequently, in the exigencies of our present civilisation, such infants are separated from their mothers and have to be tested alone.

Among *the advantages of the present micro-technique*, besides its quick accuracy and its ease to hand and to eye, may be mentioned: (1) Its importance for the testing of marasmic infants. (2) Its allowing various important multiple tests, for instance the week after week use of control samples, and of the necessarily small

samples of known positive sera proposed by Dr. D'Este Emery to be distributed as an aid to the standardisation of the Wassermann test. (3) The technique succeeds with the small volume of constant "complement" or complements obtainable, *e.g.*, weekly from one of two or more healthy male cavies. (4) The small total quantity per tube allows the use throughout of the inexpensive small apparatus that is often the only admissible in small laboratories nowadays. (5) The technique includes a simple method of taking from a merely capillary area sterile blood suitable for various purposes; and (6) it includes the simplest and cheapest method of providing sterile measuring pipettes in large numbers.

A Brief Outline of the Drop-measuring Method.

The method of drop-measuring liquids and suspensions was communicated in brief summary in 1912 to the Royal Society. Then in war-time arose opportunity to publish further matter of my original notes and of further-worked-out applications, as "A Method of Drop-measuring Liquids" in the *Lancet*, 1915, ii, p. 1243, and 1916, ii, pp. 423, 994.

Drop-measuring is the oldest known way of measuring small quantities of liquids and was copied from Mother Nature herself. But apparently only recently, in 1912, has there been published a simple precise method of uniformly gauging ordinary drawn-out pipettes to yield drops of any required volume. Drop-measuring is the only method of freely delivering small volumes of liquids and suspensions with accuracy and in the circular drop-film suitable for counting *e.g.* red blood-cells and bacteria, and its advantages are increasingly great as the volumes become smaller. Moreover, it is largely an automatic method, economising effort as well as time.

The size of a drop delivered by a clean pipette with nearly cylindrical drawn-out point held vertical depends on the outer circumference of the point at the level where the drop clings round it. The outer circumference of the point can be accurately and quickly gauged by means of an ordinary steel-plate wire-gauge with gauge holes. The drawn-out capillary is gently pushed down into the suitable hole until arrested, and the capillary is then cut close *above* the steel plate with a glass-cutting knife. The piece of capillary now remaining in the

hole may be nipped off by the nails below the plate to a stout little length, which is then easily forced, by gentle tapping, back upward out of the plate. If at any time a fragment sticks in the hole it must of course be pushed out clear by a wire.

The gauge to which a corresponding table of drop-sizes has been worked out in my 1916 *Lancet* article is the Morse drill and wire-gauge and the very similar Stubs (Lancashire) gauge. (The gauge-plate must of course be carefully cleaned with benzine. Both it and the pipettes must be carefully kept from contact with anything greasy or even "sweaty.")

The pipette sizes, Morse 77 to Morse 51, chosen for this technique are not too large to be drawn in an ordinary bunsen flame. Also, being small enough to have the drop clinging round a contact circle just above the orifice, they need not have the orifice cut off quite "square." They are cut by sawing the knife gently round the pipette till it falls by its own weight into the hand, or better, into a box lined with filter-paper and absorbent wool.

The dropping-pipettes are so easily and cheaply made that, to prevent the distraction of tedious expensive washing while setting up the test, a pipette of a suitable gauge can be reserved for each ingredient. Such assorted pipettes from ordinary tubing 5 to 6 mm. outer diameter can easily be plainly etch-marked as described below, and kept in a dust-proof cardboard box with notched racks. After use, as soon as convenient, each pipette may have its point and its inside rinsed with distilled water and then saline, and shaken so as to leave soon merely a film of brine and then of salt (which just before use can easily be rinsed out).

The case of etch-marked pipettes will include: M. 77 for saline, M. 77 for amboceptor 1 in 1000, and M. 54 or 55 (as found by small measure-flask most suitable from the worker's way of making and of using them) for r.b.c. without amboceptor; M. 79 for saline, M. 79 for titrable complement dilutions, M. 54 or 55 for r.b.c. with amboceptor, M. 51 or 52 for dilute antigen; M. 54 or 55 for the complement dilution used in the test. Also three 1 c.c. graduated capillary pipettes, for saline, r.b.c., and antigen respectively.

Another box will contain reserved tubes about 5 c.c., etch-marked, in suitable abbreviations, for S. (saline), S. Am. (saline for rinsing amboceptor pipettes), so also S. Ag., S.C., Am. 1 in 1000, r.b.c.

5 per cent., C. 1 in 2, C. 1 in 40, C. 1 in 16, C. 1 in . . . , r.b.c. + Am., Ag. 1 in 15.

For measuring the two 10 c.mm. drops of each serum to its tubes a separate tiny pipette is used and then thrown away. Two such small pipettes are in about a minute altogether drawn from a piece of tubing about 7 cm. long and 3 mm. outer diameter and gauged M. 76. The box full of them and its lid ought of course to be marked to distinguish from one or two other useful small stock sizes. Such pipettes for test sera, and for amboceptor, had better be plugged with previously ignited asbestos wool, and so plugged they may easily be sterilised, either in the hot-air oven, or rapidly, point up, over a bunsen. This seems to be the easiest and cheapest way of providing clean sterile measuring-pipettes in large numbers.

Indelible easily read non-cracking marking on the body of dropping pipettes, on mixing tubes for ingredients and especially on serum-heating pipettes has an importance well emphasised by Fildes in his 1917 Wassermann paper in the *Lancet*. Such marking may easily be done with *a simple heat-etching ink* quite harmless to glass in the cold. It consists of ordinary blue-black ink, *e.g.* Stephens' ink, to which has been added 10 per cent. of a neutral "alkaline" citrate or acetate, *e.g.*, potassium citrate, preferably along with 2 or 3 per cent. of boric acid and lead nitrate. The ink is shaken before writing on the slightly heated glass. The writing, fully visible from the first, is heated dull red by slightly rotating the part in a smoky bunsen flame. By the K_2CO_3 and possibly traces of KOH formed the glass is at once visibly and sharply etched. The frosting is even more striking after heating in water. Marking of drop-measure flasks may be done by an engraver's "India" corundum pencil, one end of which has been sharpened to a point on a carborundum stone and the other end left with sharp edges.

Uniform dropping may be comfortably secured by "steadying the ulnar edge of the thumb-tip against the radial edge of the forefinger with the teat-fundus collapsed between them, compression of the teat being accomplished by rolling more and more of the thumb-pulp over the forefinger, and inflation by rolling contrariwise." The worker's arm may be steadied on a rest.

A careful worker will duly check his work by dropping into a tiny drop-measuring flask of, *e.g.*, 0·7 c.c. capacity with short neck of about

4·5 mm. internal diameter as described in my *Lancet* 1916 article. This simple procedure finds, as it were, the resultant of the interplay of the various factors affecting the drop-volume, namely, (*a*) The circumference of the point where the drop clings round it—this factor "including" taper and position-slope. (*b*) The surface tension of the liquid—this "including" temperature. (*c*) The initial velocity of the drop—this "including" rate and steadiness of dropping.

Contact with or droppings from greasy tubes or even the fingers ought to be avoided. A pipette so soiled ought to be rinsed and wiped with alcoholic potash, and then thoroughly rinsed, first by means of a tight perforated rubber plug in the tap and then with distilled water or with saline.

Preparations for the Test.

The test-tubes used in titrating and in the tests are conveniently about 5 cm. by 8 or 9 mm., with bottom hemispherical to facilitate mixing and cleaning, and with a lip of about 3 mm. Convenient cheap racks are simply made by bending a piece of tinned copper strip about 24 in. long to form a four-sided stand $9\frac{1}{2}$ in. long and $2\frac{1}{2}$ in. high, with a lap of $\frac{1}{2}$ in. at one end fastened by a rivet. The upper length has a single row of a dozen holes just large enough to allow the tubes, when the rack is shaken, to swing suitably as they hang supported by the lip. The middle interval may be left wide enough to hold the rack by one finger. The bottom length, above which the tubes hang clear, may have a slip of white paper laid on it in observing hæmolysis and residual deposit of red blood-corpuscles.

Patient's serum may easily be taken sterile through a capillary region from a warm venously congested limb. The capillary region —in adults above the thumb-nail, in young children above the big-toe-nail, in infants the heel—is swabbed with alcohol and with ether, then well dried before a fire. Congestion is produced either by bandaging the limb from above down, if there is debility, or if several c.c. of blood is required, or by simply tying a couple of bandage turns above the elbow (over the sleeve) or above the knee. The capillary area is painted with suitably warm (70° C.) previously sterilised paraffin of m.p. 55° C. Then with a straight Hagedorn

needle, sharpened to a stub spear-point, a prick is made through the paraffin, and a sterile Wright's capsule is promptly applied to drain off the spherical drop of blood as it wells up, rhythmic pressure, if necessary, being made to promote the flow. (Mineral wax suits well.)

The Wright's pipettes are conveniently made of tubing about 3·5 mm. internal diameter, so that the blood may flow in them only plunger-wise.

Pipetting-off and heating the serum are advantageously done forthwith, as advised in Abel's *Bacteriologisches Taschenbuch*, especially if the blood is not sterile. After sealing the Wright's pipette and centrifuging, the serum is taken off into an already etch-numbered Pasteur pipette, of the same-sized tubing as the Wright's capsules, with capillary 4 or 5 cm. long. If now any r.b.c. have been taken up, the pipette is centrifuged in a long bucket, the upper end is flamed, the plug is withdrawn by the tip of a "mouse-tail" file, and the clear serum is drawn off into another numbered pipette (or if, *e.g.*, the serum is to be tested immediately after the "forthwith-heating," then, after centrifuging, the pipette is held horizontal, the part containing the r.b.c. is cut off, and by means of a bit of rubber tube slipped on to the pipette and used as a "holed teat" the serum is held back from the point in re-sealing. Contamination in cutting may be avoided by lightly flaming the scratched ring before breaking off).

In the lack of a proper water-bath the pipettes of clear serum, held together by a rubber band, may be inactivated in a closed jar of, *e. g.*, distilled water (if possibly-disturbing "antichlor" in the tap-water is to be avoided), brought to 56° C., and placed on a clean metal plate in a paraffin oven. After half an hour at 55° C. the pipettes are rinsed in distilled water and transferred to the ice-chest till required.

On the "*harmless*" *taking of the complement* mentioned in paragraph 1 a few suggestions may be made here. Such taking of blood must be from a superficial source such as the ear. Frequent cordipuncture seems a comparatively harsh procedure under which the cavy's health may suffer. And the quantity of blood, ½ to 1½ grm., caught easily from a good cavy's ear, suffices for the test of 15 to 45 or more sera by such a micro-technique as is here described. The cavies, healthy adult males, ought to be thoroughly well kept, preferably close to the laboratory itself. Complement-

taker and assistant ought to be very good friends with them. For the bleeding, almost painless in the absence of fear, the only restraining apparatus may be a clean duster pinned round the cavy's neck and wrapped round limbs and body in the assistant's hands. Warming the ears by a carbon lamp, as recommended in Muir and Ritchie's *Bacteriology*, is useful, especially after the chilly ether-swabbing. After a quick application of a suitable sharp point the thin round tube-edge pressed gently on the vein proximal to the opening, with suitable counter-pressure from a pad of cotton-wool held inside the auricle, collects the blood in the tare-marked light tube, in which it may be centrifuged.

Titration of the Reagents.

The method of transposing Fildes and McIntosh's technique (as the technique is set out in the *Lancet*, 1916, ii, October 28th, and in M.R.C. Interim Report, No. 1, on the Wasserman Test, 1918, pp. 32–35), may, in the as yet paucity of such transposings, be of interest towards the transposing of other techniques.

In setting up the various tests outlined below, each rack ought to be *shaken* as soon as each ingredient is added to it, and also every ten minutes or so while hæmolysis is proceeding.

Standardisation of the amboceptor.—Occasional.

To be repeated with the serum of at least one other cavy.

Required: (*a*) Saline, as always, fresh made, from preferably fresh-distilled water + 0·85 per cent. NaCl.

(*b*) Tube containing complement 1 in 2, *i. e.* 50 c.mm. (5 M. 76) of cavy serum with 50 c.mm. (5 M. 77) of saline.

(*c*) Tube containing amboceptor 1 in 1000, *i. e.* amboceptor 10 c.mm. (1 M. 76) mixed in 10 c.c. saline.

(*d*) Tube containing 5 per cent. sheep's r.b.c. (saline 3·8 c.c. by graduated 1 c.c. pipette and, rinsed into it, 0·2 c.c. of centrifuged, *e. g.* formalined, washed sheep's r.b.c.), preferably colour-titrated as described later.

(*e*) Pipettes including M. 76 and M. 77.

(*f*) Small rack with nine tubes 1 to 9 to receive:

amboceptor 1 in 1000	(c.mm.	10,	20,	30,	.	.	.	80,	90)
	M. 77	1,	2,	3,	.	.	.	8,	9
equalised with saline	M. 77	8,	7,	6,	.	.	.	1,	0

Complement 1 in 2 (10 c.mm.) 1 M. 76 into each tube.

R.b.c. 5. per cent. (50 c.mm.) 2 M. 54 into each tube.

Incubate one hour at 37° C. The weakest tube quite lysed contains the micro minimal hæmolytic dose (m.M.H.D.).

Estimation of the hæmolytic dose of complement, with and without antigen, is slightly less easy to transpose. But in this micro-technique the estimation of the complement-titre need only occasionally be made if the titre of the cavy or cavies is once ascertained, though as an extra control it may be performed at the same time as the actual Wassermann test.

Required: Etch-marked pipettes and mixing tubes, as specified above.

Water-bath and rack of test-tubes. In the lack of a proper thermostat this micro-technique is well served by a cubical 4-in. tin nearly full of water, with thermometer, over the by-pass flame of a bunsen. Twelve test-tubes are conveniently held in two ranks of six holes each, in a thin bit of wood or metal, to rest like a lid on the "bath." (Six tubes in each row are no more trouble by this method, and the supernumeraries give further interesting if not necessary information.) The complement is to be titrated against the actual sensitised sheep's r.b.c. suspension and the actual antigen dilution that are used in the Wassermann test. So the making up of these may be conveniently taken before the complement-diluting is transposed. But if the complement-titre of the day's cavy is already known, the sensitised r.b.c. suspension may be made up while the first stage of the test is already being incubated for complement-fixation.

Making up the sensitised r.b.c. suspension.—Of the amboceptor used (B. W. & Co.'s) the dilution is, say, 1 in 2000 with the test ingredients in the same proportions as used here.

So, to give 1 m.M.H.D. in $\frac{1}{20}$ c.c. of sensitised r.b.c., 1 m.M.H.D. will be $\frac{1}{40000}$ c.c.

But, as shown by Griffith and Scott (*Technique of the Wassermann Reaction*—Ministry of Health, 1920, p. 12), it is advantageous to use the maximum-sensitisation amount, namely 10 m.M.H.D. Accordingly in this technique is used $\frac{1}{4000}$ c.c., *i.e.* $\frac{1}{4}$ c.mm. of amboceptor, per tube.

Now, if our batch consists of 72 tubes in all, we shall need $72 \times \frac{1}{4}$,

i. e. 18 c.mm. of amboceptor. This is well included in 2 M. 76, *i. e.* in 20 c.mm. of amboceptor, which will make 80 doses each in $\frac{1}{20}$ c.c., *i. e.* in 4 c.c. altogether of sensitised r.b.c. suspension, made up thus: Into the 5 c.c. tube marked "Amb. + r.b.c." is measured 1·98 c.c. saline, by its 1 c.c. capillary pipette and 0·02 c.c. amboceptor, either as 2 M. 76 drops and shaking or by drawing up into a capillary pipette, corrected for contained amount, exactly 20 c.mm. (preferably without having to draw back the column to the mark, which procedure gives a false idea of correctness), and rinsing out into the saline. Then into another 5 c.c. tube, marked "r.b.c. 5 per cent," is measured by the saline pipette 3·64 c.c. saline, then by the r.b.c. capillary pipette 0·36 c.c. of just suitably-flowing formalined sheep's r.b.c.-deposit is rinsed into the saline. *The strength of this suspension may be adjusted* so that 0·5 c.c. of it rinsed into a total volume of 13 c.c. of distilled water will in Oliver's hæmoglobinometer read "50 per cent Hb." Then 2 c.c. of the adjusted suspension, mixed quickly and thoroughly, by pouring, with the 2 c.c. of amboceptor solution will give a practically standard sensitised suspension. (If one's centrifuge will give quickly a measurable deposit of r.b.c. of constant strength, then the slight trouble of standardising by hæmoglobinometer may be saved.)

For *the antigen dilution* 1 in 15 take, in an alcohol-rinsed capillary pipette kept for antigen, 0·15 c.c. of heart extract and 0·1 c.c. of 1 per cent. cholesterin solution (as described by Fildes and McIntosh), deliver into a dry tube, then run in 3·5 c.c. saline and shake.

Transposition of the Complement Titration.

The strongest F. and M. micro-tube of complement in presence of antigen, namely the rear fourth tube, is to contain: saline 0·02, complement 0·03, antigen 0·05 c.c. And in both racks the common micro-increment from tube to tube is to be 0·005 c.c. of complement 2 in 19. Now this 5 c.mm. would be a smaller drop than corresponds to the smallest hole in the calibrated gauge. Therefore we dilute the complement further so as to use a larger drop. In the fourth tube with least added saline we have still 0·02 of it to add to complement 0·03 c.c. Thus we may dilute the 2 in 19 complement just $\frac{5}{3}$ further, making 2 in $19 \times \frac{5}{3}$, *i. e.* 2 in $\frac{95}{3}$ or 6 in 95, *i. e.* 1 in 16 nearly, and the drop $5 \times \frac{5}{3}$, *i. e.* 8·3 c.mm. Now in the table of drop-sizes in the *Lancet*

1916 paper, 8·2 c.mm. corresponds to M. 79. So this pipette will suit —indeed for both our adjusted dilutions 1 in 16 and 1 in 16 × $\frac{5}{2}$, *i.e.* 1 in 40, the series of volumes being the same in both "ranks." In the rear fourth tube mentioned the volume of complement, 30 c.mm., is just six times the common increment, 5 c.mm. So the common increment, now 1 M. 79 of 1 in 16, and also the doses being now only diluted but not otherwise altered, the rear fourth tube will get 6 M. 79, the third tube will get 5 M. 79, and so on, of complement 1 in 16 (complement 30 c.mm., *i.e.* 3 M. 79 + saline 0·45 c.c.). And the front rank tubes will get the same series of volumes of complement 1 in 40 (complement 10 c.mm., *i.e.* 1 M. 79 + saline 0·39).

The front rank, complement without antigen, will have :

Complement, 1 in 40, M. 79 : 2, 3, 4, 5, 6, 7.
Saline, to 100 c.mm. M. 79 : 10, 9, 8, 7, 6, 5.
R.b.c. and amboceptor 50 c.mm., *i.e.* 2 M. 54 to each tube.

The rear rank, complement with antigen, will have :

Complement, 1 in 16, M. 79 : 2, 3, 4, 5, 6, 7.
Saline, to 50 c.mm. M. 79 : 4, 3, 2, 1, 0, 0.
Antigen, 1 in 15, 50 c.mm., *i.e.* 2 M. 51 to each tube.

Place all in the water-bath at 37°C. for ten minutes or so with occasional inspection and shaking. By about this time the front F. and M. "fourth" tube ought to be completely lysed : if not this cavy is already proved unsuitable for the Wassermann test. If lysis is so far satisfactory, dry the tubes roughly by touching with blotting-paper and support the rack on a dry tin already warm in the incubator for the rest of the hour, with occasional inspection and shaking. Now, note the front rank m. M.H.D. Put in each back tube 50 c.mm., *i.e.* 2 M. 54 of r.b.c. and amboceptor, and place as before in the water-bath for 10 minutes. If now the complement-weakest tube in the four tubes of the back rank is the same in order as the front rank tube already noted or if it is just one tube stronger note it : the complement is satisfactory. (But if the complement is not thus satisfactory then test another cavy.)

Reckoning the complement dilution for the test.—If the tubes "noted" are (as rarely) the front and the rear tubes of the *first* F. and M. file, or if they are the first F. and M. rear tube and our front supernumerary, then the amount of actual complement to be dosed to each tube in the Wassermann test is the amount in the rear tube +

half the amount in the tube in front of it, *i.e.* $3 \times 8{\cdot}3$ c.mm. of 6 in 95 dilution + $\frac{1}{5}$ of that amount, *i.e.* altogether the amount $\times \frac{6}{5}$, *i.e.* $\frac{3}{1} \times \frac{25}{3} \times \frac{6}{95} \times \frac{6}{5}$ c.mm., and since it is to be contained in 50 c.mm., then 1 c.mm. of complement will be contained in 50 divided by that number, *i.e.* in $50 \times \frac{3}{25} \times \frac{95}{6} \times \frac{5}{6} \times \frac{1}{3}$, *i.e.* $\frac{4\,75}{6} \times \frac{1}{5}$, *i.e.* $\frac{79{\cdot}2}{3}$, *i.e.*, in $26{\cdot}4$ c.c., *i.e.*, the dilution is 1 in $26{\cdot}4$. Similarly if the second rear tube is "noted," the dilution is 1 in $\frac{79{\cdot}2}{4}$, *i.e.* 1 in $19{\cdot}8$. If the third, 1 in $\frac{79{\cdot}2}{5}$, *i.e.* 1 in $15{\cdot}85$. If the fourth, 1 in $\frac{79{\cdot}2}{6}$, *i.e.* 1 in $13{\cdot}2$.

The Test Proper.

Required: Racks of test-tubes as described, charged as described below by the etch-marked pipettes. Sensitised r.b.c. suspension and dilute antigen and saline as for use in complement titration.

The required complement dilution: If the cavy's serum has been found to require a dilution of, say, 1 in $15{\cdot}8$ for a volume of $\frac{1}{20}$ c.c. to each tube, then for the 60 tubes of the test we need $60 \times \frac{1}{20} \times \frac{1}{15{\cdot}8}$ c.c., *i.e.* $\frac{3}{15{\cdot}8}$ c.c., *i.e.* nearly 200 c.mm., *i.e.* nearly 20 M. 76 of complement. By an asbestos-plugged small M. 76 pipette with body 3 to 5 cm. long pipette off, say, 24 M. 76 of clear complement and dilute in $0{\cdot}24 \times 14{\cdot}8$, *i.e.* in $3{\cdot}55$ c.c. saline in the tube marked "C. 1 in . . ." ready for dosing in the test.

Setting up the Test.

Have the 60 tubes for the test set up in single rank in five racks of a dozen each, marked off by a transverse stroke between the pairs, and the number of each serum marked between its tubes in grease pencil on the tinned-copper top-plate. Set out in the same order all the plainly numbered serum-pipettes in every second groove of a strip of corrugated packing-card. Now for each serum in turn put a small M. 76 pipette, plugged and sterile, into a small teat (fitting neatly by means of a few turns of a tiny rubber band passed round its neck to form a sphincter, which is rolled to the neck of the teat while the pipette is being held airtight). Working the teat as suggested above, fill the M. 76 from the upper end, flamed and unplugged, of the first serum pipette, and deliver one drop each to its two tubes, then seal the upper end of the numbered pipette. Roll the teat-sphincter back, slip out the first M. 76, and lay it in the groove just to the right of its numbered pipette, to

indicate that that pipette has been "distributed." Then insert a second small M. 76 in the teat, and so on. Each "test" tube, hanging clear by its lip, shows clearly whether it has duly received its drop.

Schema of Micro-Wassermann Test.

	"Test."	"Control."
Serum	1 M. 76 (10 c.mm.)	1 M. 76
or c.s.f.	2 M. 77 (20 c.mm.)	2 M. 77
Saline	—	2 M. 55 (50 c.mm.)
Complement dilution	2 M. 54 (50 c.mm.)	2 M. 54
Antigen 1 in 15	2 M. 51 (50 c.mm.)	—
Incubate 1 hour at 37°C. Then add		
R.b.c. + amboceptor	2 M. 54 (50 c.mm.)	2 M. 54
Water-bath at 37°C. for about 15 minutes.		
Read. Ice-chest for an hour or more, then read again.		

Sundry Observations on the Test.

The schema of the test shows the amount and the order of adding the remaining reagents. Control-dropping into a tiny drop-measure flask will decide whether an M. 54 or an M. 55 pipette with the particular drawing of capillary and with the way of dropping attained is the more exact. During the stage of hæmolysis fairly frequent observations, and occasional shakings, are useful to show not only the result in each tube, but also the rate at which the result was reached. Completeness of hæmolysis in a shaken tube is shown by, *e.g.* sharpness of the lamp-filament-image formed by the tube. The degree of hæmolysis when incomplete may be roughly estimated by the shade of clear red, especially with the help of standard tubes and also by the size of any deposit of r.b.c. shown from above at the bottom of the tube over a white paper.

The tiny masses in the tubes have the advantage of warming up rapidly. A bath is hardly necessary for stage 2 of the test, and it may in case of need be only a tinned copper dish, 10 × 10 × 3 in. with squat pyramid lid, heated at 37°C. over two small flames. The slight convection-evaporation during the first stage may be lessened by covering the tube-mouths in each rack with a strip of filter-paper pressed down by cotton-wool and a strip of wood laid on it.

C.s.f. has nearly the same drop-size as water, and, by the way, does not need inactivation. It is used in a dose double that of serum.

P.M. sera—successfully tested in large numbers by McIntosh and Fildes—require only half dose of antigen.

A quantity of serum only $\frac{1}{100}$ c.c. may be made to suffice for test and control by using $\frac{1}{200}$ scale instead of $\frac{1}{10}$ scale. The serum is measured as drops of 5 c.mm. by fine capillary pipettes gauged in a suitable hole of a "drawplate," which hole will have to be calibrated by the worker, by low-power microscope-micrometer measurement of holes and of capillary, and by dropping from the pipettes into a small drop-measure flask. After getting the tiny serum pipettes, the rest of the test is even slightly easier than on $\frac{1}{10}$ scale, inasmuch as of the other ingredients only one of each two drops in the schema has to be distributed to each tube.

Summary.

The special feature of this method is to use in the successive batches of tests complement of known suitable titre from an ear vessel of one or more duly titrated cavies, which cavies with good treatment will do service for at least a couple of years. Standardisation of the Wassermann test is largely secured by the use thus of identical complement "on tap," instead of the use of a succession of various only-once-used complements from donors that can give no more. "Of all the reagents in the Wassermann reaction complement is the least capable of standardisation, and it is certainly the reagent which is most often responsible for discrepancies in the results on different occasions."

Incidentally the use thus of an already titrated cavy saves about ninety minutes per batch of tests.

The involved standardisation of the red-cells suspension is easily carried out by hæmoglobinometer.

The article has a necessarily detailed account of the "hall-marked" drop-measuring micro-technique, by means of which was worked out the feasibility of thus using repeatedly a titrated cavy. The micro-technique furnishes most simply, cheaply and compactly a supply of sterile individual measuring-pipettes for the sera to be tested. The sera are taken sterile from a pricked capillary area coated with sterile paraffin wax.

Important among the details of technique is a simple harmless instantaneously heat-etching ink for inactivating-pipettes.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

Meeting held on November 16th, 1922, Dr. H. G. Adamson, President of the Section, in the Chair.

Dr. W. Jenkins Oliver showed a *case for diagnosis.* Girl, aged 7 years, in apparently good general health. The skin lesions were confined to the back and right flank, and consisted of five round and irregularly quadrilateral erythematous macules, some of which showed fine scaling. The lesion on the back of the right shoulder differed from the others in being darker in colour, of a slightly bluish tint with a white shade in the centre. Over this, the oldest macule, there was, on palpation, the suggestion of a lack of suppleness of the skin which was not apparent over the other lesions. The duration of the various lesions had been: (1) Back of right shoulder, eighteen months; (2) small round patch on left side of spinal column over scapular region, fifteen months; (3) one round and one large irregularly shaped area extending on to the right flank, about ten months; and (4) irregular quadrilateral lesion over right sacro-iliac region, four months. Since their first observation the spots, according to the mother's statement, had appeared to become larger, especially the one on the right flank. The oldest lesion on the right scapula had always been different from the others, with its white centre. There was no history of trauma, nor of drug-taking. Neither the patient nor the parents had been abroad, and there was no apparent alteration of sensibility over any of the macular patches, while the child complained only of some occasional irritation about them. He showed the case as one for diagnosis, putting forward the tentative suggestion of localised scleroderma, in which case the purely erythematous macules showed how slow may be the evolution of the sclerodermatous condition.

Dr. H. G. Adamson (President) said that this type of scleroderma with one or more oval patches generally on the back was not uncommon in children. They were sometimes associated with erythematous rashes or urticaria, and more rarely with fluid in the joints—evidence perhaps of a general toxæmia. The erythematous patches in Dr. Oliver's case were, he thought, an early stage of the scleroderma;

they had the peculiar lilac colour of the spreading margin of a sclerodermic patch and already showed sclerodermic changes to a slight degree. The prognosis in this type of case he regarded as good. He had not found that any form of treatment had any good result, but the sclerodermia patches often disappeared spontaneously in course of time.

Dr. Graham Little said that he showed a similar case in a child, aged 9 years. The condition was on the back, and there was a very distinct history of acute onset. The eruption appeared during the time she was attending the hospital, a patch the size of a half-crown developing in three weeks, and there was an erythematous blush, as in this case. Three of the patches underwent spontaneous involution in six months, leaving no trace whatever.

Dr. S. E. Dore said he thought the erythema stage of sclerodermia was not sufficiently recognised. The patient in a case which was under his care gave a history of recurrent attacks of "eczema," but they were attacks of erythema preceding the sclerodermia. The sclerodermic patches were not only preceded by a margin of erythema before they spread, but she had localised patches of erythema, which eventually became sclerodermatous patches.

Dr. J. B. Christopherson showed a case of *leishmaniasis of the skin resembling lupus vulgaris*. The case was, in his opinion, one of an hitherto unclassified form of leishmaniasis of the skin, resembling lupus vulgaris. It was shown on July 20th, 1922. Of the speakers on that occasion Dr. Whitfield alone agreed with the diagnosis of leishmaniasis. The patient, a staff nurse, was bitten on the cheek by a biting fly whilst doing hospital work with the army at Baghdad in September, 1920, and a small single sore formed. Being invalided for tachycardia, she was sent to Netley Military Hospital, where the sore was investigated, Leishman-Donovan bodies found, and the lesion was diagnosed as Baghdad or Oriental sore. It gradually improved under treatment with methylene-blue ointment and antimony ointment (no intravenous injections were given); the X-rays were applied once. It never completely disappeared, and in June, 1922 (a year after her discharge from Netley apparently cured), she came before a medical board and was sent to the tropical diseases clinic.

On June 9th of this year, when she began to receive intravenous injections of antimony tartrate, there were about twenty-five vesicular lumps of varying sizes, which, when taken between finger and thumb, looked yellow and round, and were soft. The skin over the lumps was not ulcerated or broken. The nodules, when punctured, were found to be hollow, and were filled with an apple-jelly-like content, similar to what was found in lupus vulgaris. These nodules were grouped around the scar of the original Oriental sore. To-day the

lumps had vanished, the area of skin occupied by the vesicular nodules was level with the surrounding skin, and the nodules themselves were not much more than mere stainings.

He did not think that lupus vulgaris would have shown the improvement this condition had shown in three months under any circumstances whatever. The patient was practically well four months after treatment with intravenous sodium antimonium tartrate commenced; given in single doses, commencing with $\frac{1}{2}$ gr., increasing to 2 gr. per dose, a course of 30 gr. was administered at first, and, after an interval of two months a subsidiary course of 12 gr. had been given.

He might say that Leishman-Donovan bodies were found in the original single Oriental sore, one and a half years ago, which apparently healed, and degenerated Leishman-Donovan bodies were found in the nodular sore which he described to-night. Also "blue-bodies" were found abundantly in the smears. Blue-bodies were round bodies of variable size which stained a uniform blue colour with methylene-blue, apparently structureless; they were found invariably in smears and sections of leishmaniasis specimens. He was the more inclined to the diagnosis of leishmaniasis because this was not the only case of the kind he had seen. He had another case, similar to this one, under observation; the patient was also a nurse, and also from Baghdad: in her case, too, the nodular sore occurred on the face; and another point of similarity between the two cases was that the sore on the face, appearing after the original sore, on the arm in the second case, had been apparently cured for some time.

Now the clinical story in these two cases was suggestive of an imperfectly cured or residual condition, or perhaps a modified form of leishmaniasis, the variation of which from type was due to treatment. In neither of these cases was the original sore treated with intravenous injections of antimony tartrate. In both cases the Leishman-Donovan bodies were either absent or difficult to demonstrate, but there was no doubt about the case he showed to-night being very susceptible to the specific remedy of leishmaniasis—intravenous injections of antimony tartrate. There was no doubt also about the lesion being very similar in appearance to lupus vulgaris, and he described it as leishmaniasis of the skin assuming a lupoid form.

Dr. J. M. H. MacLeod said that he thought the appearance of the lesion suggested that the leishmaniasis might have become secondarily infected with tubercle, as the lesion was indistinguishable from lupus in its appearance. He would have liked to have seen a section, as it might have assisted in solving a problem.

Dr. Arthur Whitfield said he had examined sections from a case of what afterwards proved to be leishmaniasis, and he found himself unable to diagnose, under the microscope, the non-ulcerated leishmaniasis from one type of lupus. He had, indeed, made the diagnosis of lupus in a case which afterwards was shown to be leishmaniasis. It would be of help if sodium antimonium tartrate were tried by injection in cases of undoubted tubercular lupus, as this might show that the beneficial result obtained in this case could not be obtained in lupus. He believed antimony had been used for the condition by giving it freely *per os* many years ago, before Koch's first tuberculin came out, because it was stated a reaction could be caused by giving large doses of arsenic or of antimony.

Mr. McDonagh said he had seen three cases of leishmaniasis in which after the disappearance of the primary lesion papules appeared in the periphery. These papules were the result of direct spread along the lymphatics from the original focus, as was proved by serial sections. Unless the phases of the life-cycle of the organism were demonstrable in a section it was impossible to differentiate between leishmaniasis, tubercle, syphilis, etc., as these diseases were capable of producing the same histological picture. Development of papules by direct extension from the primary lesion which was so common in syphilis was not at all rare in the condition under discussion.*

Dr. H. C. Semon said he had a very resistant case of lupus vulgaris of the nose which he had had treated by Finsen light. It was not very successful, and the patient came back twice with recurrence after apparent cure. Dr. Christopherson and he then tried a course of antimony injections by way of comparing its effects with those achieved in the nursing sister's case. He did not think there had been any improvement, and certainly not to the degree shown by the case presented by Dr. Christopherson.

Dr. Christopherson (in reply) said that this case was tried with the intravenous injection of sodium antimonium tartrate, with the idea it possibly might be lupus vulgaris. The question of making a section from the lesion was put to the patient, but as the condition was obviously getting well, it did not seem quite fair to do a biopsy, especially as the site of the sore was a conspicuous one. Animal injections were not thought of until too late. Typical Leishman-Donovan bodies had not been seen in this case in June—five months—when the warty appearance occurred, but this was not altogether against the diagnosis of leishmaniasis; in a number of other diseases one was not always able to find the causal organism. In the present case "blue bodies" had been found repeatedly, and these he looked upon as almost diagnostic of leishmaniasis. Some were degenerated Leishman-Donovan bodies, some no doubt the cytoplasm of tissue cells broken up by the Leishman-Donovan bodies.

Dr. E. G. Graham Little showed a case of *folliculitis decalvans*. The patient was a lady, aged 57 years. He thought it was a case of

* See *Brit. Journ. Derm.*, 1915, xxvii, p. 91; 1921, xxxiii, p. 182.

the pseudo-pelade of Brocq, for although there was very little evidence of active folliculitis, there was a peri-follicular ring round several of the hairs, giving the coarse "orange rind" aspect of the skin which was often found in Brocq's pseudo-pelade. Whether it was desirable to make this type a separate entity from folliculitis decalvans was a matter of opinion. In one of their discussions Dr. Pringle pressed for the non-separation of cases of pseudo-pelade from the class of folliculitis decalvans, unless they reserved the former name for differentiation of a group of these cases showing definite atrophy, but without a very active suppurative stage. He would be glad if it could be shown that this was a more hopeful form of alopecia. It was still extending in this patient. She had had thinning of the hair for a number of years, but it was only distinctly noticeable from last July. She had also a long history of what was probably colitis, dating from a visit to Buxton eleven years ago, when there was, at that watering place, an epidemic of choleraic diarrhœa, probably from a food-poisoning infection. She had ever since had an inflammatory condition of her intestinal mucosa, and her custom had been to have several loose motions per day. That part of her trouble, however, had now been materially improved by adopting Dr. Guelpa's treatment. He did not know whether the colitis was related to the skin condition.

Dr. S. E. Dore said he did not contest the diagnosis in this case, but it did not resemble any case of pseudo-pelade he had seen; it was much more diffuse. Generally the transition between the cicatricial area and the normal hair was more abrupt. He had now under his care two patients with lupus erythematosus affecting the scalp without any lesions on the face or body, and it was possible that the case under consideration might be an instance of this disease.

Dr. Douglas Heath mentioned a type rarer than the diffuse variety, in which there were patches with a swelling round the affected hairs, and the hairs broke off short, as in alopecia areata. The swelling was marked, and there was itching and irritation; the hairs fell out, and did not re-grow. The affected hairs were very œdematous; when a hair was withdrawn the sheaths were very swollen. He had not found any organism in them, though he had made many cultures. He did not know whether that condition should be grouped with the disease now being discussed.

Dr. E. G. Graham Little showed *two cases of favus of smooth skin*. The patients were a boy, aged 6 years, and a girl, aged 8 years; the former had a patch of favus on the chin, the latter on the right ear. Both had become very much better with the use of boracic ointment which he perscribed as a placebo. The ear lesion had

almost entirely cleared up. The favus fungus was very obviously present in both lesions. He had not seen a case of favus for five or six years, and the disease was increasingly rare. It was difficult to know where this was likely to have come from. The house was not infested with mice. The children were resident in London, and had been for the past three years, having originally come from India. There was no infection before they left India, and the whole of the symptoms had appeared during the last six weeks.

Dr. A. M. H. Gray said that he had been talking that day to Mr. Foulerton, of the Public Health Department, University College, who said he had recently seen a good deal of favus in mice. He (Dr. Gray) thought there was a certain amount of scalp favus about; there had been two cases at his clinic in the last few months, but the patients did not show the classical signs of the favus cups.

Dr. H. G. Adamson (President) said that unless scutula were present it was not possible to distinguish favus of the glabrous skin from tinea circinata without making a culture.

Dr. H. W. Barber showed a case of *Darier's disease*. Patient, a male, M. C—, aged 11 years, an orphan and illegitimate child. His mother had another child, a girl, by her husband; this girl was now aged 21 years, and was alive and normal. The patient's father was a single man and was not known to have had other children. Neither parent had any chronic skin disease. The eruption began more than six years ago, *i. e.* before he was 5 years old. It appeared first on the backs of the hands and on the extensor surfaces of the legs. The face had become affected only recently. The eruption involved chiefly the backs of the hands and wrists, the forehead, temples and sides of the nose, the neck, the legs below the knees, the groins and axillæ. On the forehead crusting had occurred, but the scalp was only slightly affected. The lesions on the hands and wrists resembled flat warts, and on the face the greasy appearance and follicular involvement were well seen.

Dr. J. M. H. MacLeod said he had had a very extensive case of Darier's disease under his care for a long time: the legs were badly affected. Owing to the keratinisation being so imperfect, the skin of the leg became septic and eczematised. This healed up on X-ray exposure, but no permanent effect was produced by the rays on the Darier's disease.

Dr. W. J. O'Donovan showed a case of *squamous carcinoma of face in a girl*. M. B—, a single woman, aged 24 years, first attended Dr. J. H. Sequeira's out-patients' department at the London Hospital

on January 23rd, 1920. She then presented a painless longitudinal ulcer over the right lower jaw of seven years' duration. There was a similar smaller area below her left ear. No X-rays had been applied. There was a narrow area of white scarring around the ulcer. Twenty treatments with Finsen light and the application of ointments had not produced any good results by the end of 1921. Four applications of X-rays, half to whole Sabouraud pastille doses, were also of no value, but as the patient had moved far out into the country her visits were now infrequent. By October, 1921, there was still an oval shallow ulcer on the skin over the right lower jaw, with a white highly vascularised livid margin. Thick crusting up of the ulcerated surface was a marked feature at every attendance. In July, 1922, the ulcer had a "nodular-rolled edge." To-day she presented an oval pink ulcer over the right lower jaw, 12 by 7 cm., with a narrow mixed rounded pale margin traversed by fine vessels. Below the left ear there was an irregularly shaped rounded skin lesion, pink, slightly sunken, having a definitely raised palpable margin with a smooth non-ulcerated surface. There was no adenitis. The lesions were apparently no larger than when first seen in 1920. On August 25th a portion of the edge was removed for microscopic examination.

Microscopic examination by Prof. H. M. Turnbull, M.D.—"The specimen is a portion of skin, measuring 6 mm. long by 1·5 mm. broad by 2 mm. deep, in formaldehyde solution. On the surface is a brown area (5 mm. long); the remainder of the surface is finely wrinkled.

The skin contains sebaceous glands, hair-roots and hair-follicles. In the centre of the specimen there is a depression in the epidermal surface. Broad processes of epidermis extend downwards deep into the dermis beneath this. Round these processes there is a conspicuous infiltration of the dermis with lymphocytes, occasional plasma-cells and a very few eosinophil leucocytes. Here are very many distorted cells which are represented by fusiform or thread-like pyknotic nuclei. Similarly distorted cells are present in other portions of the dermis. The papillary zone of the epidermis shows a focal area of œdematous rarefaction. Within the enlarged and elongated epidermal processes are three rounded masses of horn containing a few nuclear remnants. Similar masses of horn are seen in the mouths of hair-follicles in other parts of the section.

In the deeper portions of the processes the cells are slightly swollen, and prickle-borders are absent. Prickle-borders are distinct in the greater part of the remainder of the epidermis, but not throughout. In other respects the cells are not atypical. The outer margins of the deeper portions of the processes are irregular and very poorly defined. They are not limited by the distinct layer of basal cells which is present in the remainder of the section. The lack of definition of the processes is in part due to the margins being crossed by many of the fusiform and thread-like distorted nuclei. The elongated and downward processes of the epidermis cannot be explained by wrinkling of the skin and tangential section. They appear to be the result of overgrowth of the epidermis. The three included masses of horn suggest that the overgrowth of one process follows a tortuous hair-follicle. The growth is associated with infiltration of the adjacent dermis. The absence of the basal layer and the irregular boundary and poor definition of the processes give evidence that the overgrowth is atypical. The lack of definition is largely due to the distortion of cells, particularly infiltrating cells. The cellular distortion and the focal œdema are doubtless due to the injection of anæsthetic. Allowing for this artefact, I consider that the abnormalities in the margins of the processes make it necessary to regard the overgrowth as carcinomatous, or potentially carcinomatous."

Dr. A. Whitfield said he did not think the section taken had gone deep enough, nor was it sufficiently extensive, to enable a sound opinion to be formed. It was a chronic inflammatory trouble, and there was an immense amount of small-celled infiltration beneath; all the tissue concerned consisted of small-celled infiltration. There was also folding and a biting off of bits of epithelium. A deeper section might show something more interesting below the band of small-celled infiltration.

Dr. H. G. Adamson (President) said that the case was of great interest, in view of the instances of superficial rodent seen by the members recently. He thought this case was, clinically, exactly like those cases. There was a rolled edge, and slightly crusted or scaly centre. The extraordinary feature was that the section showed a squamous-celled growth instead of the usual basal-celled growth, such as had been described in all of the previously described cases with the same clinical type of lesion. He suggested that Dr. O'Donovan should make further microscopical sections to see whether the lesion showed a basal-celled growth in another part.

Dr. H. C. Semon showed a case of *adenoma sebaceum*. Patient, a girl, aged 13 years, had developed the soft, closely aggregated, raised

yellowish-pink waxy lesions in the nasolabial grooves and symmetrically on the cheeks when 5 years old. Small telangiectatic stigmata were also to be seen, and there was a flat warty mole in the left frontal region.

To complete the picture of the Pringle type, the child was very poorly developed mentally, could remember nothing of what she was taught at a special school, and had suffered frequently from epileptiform seizures from an early age. An uncle on the father's side was said to have died in a fit after many attacks. Microscopic sections showed embryonic hair-follicles, sebaceous and sweat glands. The Weigert stain proved the sparsity of elastic fibres, and the whole histological appearance strongly suggested the nævoid origin of the disfigurement.

It was proposed to destroy the lesions individually, in a number of sessions, by means of the electric cautery.

Dr. W. F. R. Castle showed a case of *epidermolysis bullosa*. This mother and her baby had epidermolysis bullosa. The disease could be traced through four generations, the great-grandfather, grandfather, mother and child being affected. The mother was one of eight children, all of whom were affected except the second and seventh. The second and the seventh were both married, and their children were healthy. The sixth and eighth were both married but had no children. This woman's eldest child, a boy, was born normal, but died shortly afterwards from "blisters." The second child, a daughter, was stillborn, and was covered with blisters. The third was normal. The fourth, a girl, suffered from amenorrhœa, and had mental symptoms. The mother of the child had well-marked lesions on her legs, and her Wassermann reaction was triply positive. The blisters on her ceased immediately on the birth of her child. The child also showed blisters and small white bodies on the fingers. The nails of the mother were badly affected.

Dr. S. E. Dore asked whether the scalp was ever affected in such cases. Last week he saw a girl with epidermolysis bullosa, and she had cicatricial patches on her head, looking like pseudo-pelade. She had lost the whole of the hair from her head, but it grew again except on the cicatricial patches. He presumed the latter was due to injury.

CURRENT LITERATURE.

INFLAMMATIONS, ETC.

A CASE OF FOX-FORDYCE DISEASE. Walter. (*Derm. Wochenschr.*, June 24th, 1922, lxxiv, No. 25.)

A six months' eruption of irritable papules symmetrically in the axillæ, with loss of hair in this situation, in a girl, aged 15 years, seemed to justify the diagnosis of Fox-Fordyce's disease. The opinion was borne out by the histological picture of actual increase of sweat-glands and ducts and corneous hypertrophy (parakeratosis not present). Round-celled infiltration round hair-follicles and sweat-glands was particularly noticeable.

The question of classification among the névrodermites of Brocq is discussed, and the ætiology—chronic infection of the hair and sweat-ducts by scratching—suggested.

All therapeutic measures were powerless to bring about a cure. H. C. S.

LUPUS ERYTHEMATOSUS ACUTUS DISSEMINATUS HÆMORRHAGICUS. Moses Scholtz. (*Arch. of Derm. and Syph.*, 1922, vi, p. 466.)

A case is here reported of acute disseminated lupus erythematosus in a woman, aged 31 years. The parts at first affected were the bat's-wing area of the face and a patch on the upper part of the sternum. The lesions were acutely inflamed with a turgescent border and a greasy smooth surface covered with fine, dirty white, adherent scales. They developed acutely and were associated with constitutional symptoms. Two weeks later feverish attacks developed, the patches on the face extended rapidly down on the cheeks and on to the forehead, became hæmorrhagic, and from them there was a diffuse oozing of blood. Multiple lesions appeared elsewhere on the limbs and body. After attaining its maximum, the eruption remained stationary for a week, then began to recede. During this time elevations of temperature occurred, but these ceased, and about two months after the appearance of the eruption the patient became convalescent. The improvement did not last long, however, and symptoms of kidney trouble supervened, which led to a fatal issue three months later, when it was found that she was suffering from pyonephrosis. J. M. H. M.

MUCOUS MEMBRANE AND BLOOD CHANGES IN A CASE OF DARIER'S DISEASE. Sklarz. (*Derm. Wochenschr.*, June 3rd, 1922, lxxiv, No. 22.)

In a typical case of this rare disease in an artisan, aged 43 years, who had shown signs of the malady since birth, the author describes minute white pepper-corn-size granular lesions on the hard palate. The mouth and buccal mucous membrane were otherwise unaffected.

The biopsy of the skin demonstrated the usual and particular histology characteristic of the condition to which Darier has given the name of Psorospermose folliculaire végétante. That of the mucous membrane affected revealed pronounced parakeratosis, abnormalities of the stratum corneum, an almost complete deficiency of the stratum granulosum, and considerable broadening and prolongation downwards of the interpapillary rete, with isolated small

cavity-formation in the upper layers of the Malpighian body itself. A few of the swollen rete cells bore a distant resemblance to the *corps ronds*, so characteristic of Darier's disease, but none of these could be regarded as typical examples.

The blood picture varied in the course of a week between 3½ and 3¾ million red corpuscles and 8800 and 7300 white corpuscles per c.c., of which 52 per cent. were polynuclear leucocytes, 2 per cent. eosinophile, 26 per cent. large and small lymphocytes, and 20 per cent. transitional types. In the second week this latter figure had risen to 38 per cent. of the total white count, and was not explicable on any recognised hypothesis in connection with the disease. H. C. S.

HENOCH'S PURPURA. R. J. Millard. (*Med. Journ. of Australia*, October 14th, 1922, p. 446.)

Dr. Millard reports a case of Henoch's purpura in a boy, aged 16 years, a shop assistant. The patient complained of severe pain in the abdomen and vomiting. He had been taken ill two days before admission to hospital. Considerable tenderness of the abdomen was present but not much rigidity. A scattered purpuric rash was present on the trunk and elbows.

Under general anæsthesia the abdomen was opened over McBurney's point. Abundant free sanguineous fluid was found in the peritoneal cavity. The cæcum was found to be intensely inflamed. The appendix was unaffected. An incision was made in the middle line above the umbilicus. The pancreas and gall-bladder were normal. The small intestine generally was in the same dark and congested condition as the cæcum. There was no sign of mesenteric thrombosis. Drainage was established through the original incision. Pain and vomiting ceased after the operation, and recovery was uneventful except for the development of varicella. J. H. S.

CUTANEOUS TUBERCULIN REACTIONS IN SKIN TUBERCULOSIS. K. Hübschmann. (*Ceská Dermatologie*, 1922, iii, p. 246.)

In 45 cases of various forms of skin tuberculosis (32 of lupus vulgaris) the author obtained a positive cutaneous reaction in every case. His experiences disagree with the statement of Wolff-Eisner that in lupus a negative reaction is relatively common. Cuschmann found more cases giving a positive reaction with bovine tuberculin than with human virus while Kretschmer's experience was just the reverse. The author did not have a single case giving a positive reaction with one tuberculin and a negative one with the other.

Spinka (St. Louis).

CONCERNING TUBERCULINS AND VACCINES OF COLD-BLOODED ANIMALS IN DERMATOLOGY, AND SOME THERAPEUTIC EXPERIENCES. Hübschmann. (*Ceská Dermatologie*, 1922, iii, pp. 115, 140, 177.)

The author discusses all the known forms of tuberculins, various methods of their application, the nature and types of tuberculin reactions and therapeutic methods used. From the diagnostic standpoint, the best results were obtained by a modification of von Pirquet-Petreoschky method. A double scarified cross was used; it gave a large percentage of positive, well-pronounced reactions. In dermatology, vaccines and tuberculins play, therapeutically, an important *rôle*

as accessory measures to medicinal and photo-therapy. Good results are reported in tuberculosis of mucous membranes, where subjective symptoms were promptly relieved. For ambulatory cases the author recommends Pomdorf's inunction method. Weleminsky's tuberculomucin given in injections was unsatisfactory; when used in form of compresses it usually stimulated an abundant growth of granulation-tissue (in scrofuloderma).

Chelonin (turtle vaccine) was not found to be a specific. Its beneficial effect on skin tuberculosis cannot, however, be denied. It has an advantage over the old tuberculin as it causes a less severe reaction and has a longer period of activity. SPINKA (St. Louis).

SOME FURTHER FINDINGS IN BROMODERMA. K. HÜBSCHMANN. (*Ceská Dermatologie*, 1922, iii, p. 280.)

THE author reports two cases of bromoderma that showed a decrease in the calcium content of the blood and confirmed his former expectations (6·66 to 7·77 mgrm. per cent. against 9·48 to 11·11 mgrm. per cent. of normal controls). The author recently recommended calcium therapy for bromoderma. The following ointment proved very efficient for local use:

℞ Calcii chlorati cryst. puriss, Merck . . . . . g. 10.
Solve in paux. aquæ.
Eucerini anhydr. orig. Biesdorf ad. . . . . g. 100.
Aq. calcis *q.s.* to make ung. moliss. SPINKA (St. Louis).

CONTRIBUTION TO THE THERAPY OF ACNE VULGARIS. ORHA. (*Ceská Dermatologie*, 1922, iii, p. 184.)

PROMPT and cosmetically good results were obtained in stubborn cases of acne by injections of stanoxyl. 4 c.c. doses were injected daily or three times a week. About ten doses were required. SPINKA (St. Louis).

"DE L'ERYSIPÉLOIDE." W. DUBREUILH and P. JOULIA. (*Ann. de Derm. et de Syph.*, December, 1922, pp. 609–614.)

THIS article supports the view that erysipeloid is a distinct clinical entity, with at present an unknown pathogeny. It was originally described, from cases seen in butchers, by Morrant Baker in 1873, under the name of erythema serpens. Rosenbach rechristened it, and numerous other investigators—Ohlemann, Gilchrist, etc.—have reported instances. The latter saw a large number following the bites of crabs.

The writers review five cases; four follow injuries from the bones or shells of fish, and the other a scratch by a splinter of meat bone. Two or three days later, round the wound, appears a red zone which gradually extends. Ultimately the whole of a finger, with part of the hand, may become involved. The spreading edge is slightly raised, infiltrated, painful and tender on pressure. The older portions gradually assume a dusky tint, are slightly depressed and scaly. In two or three weeks all the inflammation subsides under a simple treatment.

These are the first cases of this nature reported in French literature. It is regarded as a septic condition allied to erysipelas. It differs in the slowness of onset, absence of constitutional symptoms, and marked tendency towards recovery. The authors think that the pathogenic organism is probably anaërobic, but their cultures of the serum taken from the spreading edges of two of their cases proved negative. R. P. W.

ÆTIOLOGY OF DERMATITIS IN BAKERS. Oscar de Jong. (*Lancet*, 1923, i, p. 80.)

The writer says that this dermatitis occurs only in bakeries where the hands are used in mixing, not in bakeries where machines are used for this purpose. Investigation showed that flour was not responsible, as no cases of dermatitis were found in men employed in flour mills, though they were constantly handling flour. Similarly no cases were found in men handling or preparing yeast. Dr. de Jong says that the condition is due to immersing the hands and arms in the salt solution which is added to the flour. This is about 3·6 per cent. in strength. The salt crystallises on the arms of the workers, and the kneading forces the crystals into the skin, setting up a dermatitis in susceptible individuals.

R. P. W.

NEW GROWTHS.

HISTOGENESIS OF TAR CANCER. Bierich. (*Derm. Wochenschr.*, November 4th, 1922, lxxv, No. 44.)

Daily applications of coal tar to the skin of white mice were regularly followed, on the 40th day, by hyperkeratosis, on the 80th by epithelial hypertrophy, and on the average, on the 131st day invasion by growth of the deeper structures—epithelioma. If the tar applications are withheld in the second stage, the progress towards malignancy is not merely affected. The author concludes that the production of cancer in this instance follows certain definite laws, which are irreversible once the stage of epithelial hypertrophy has been reached.

Besides these local tar reactions there are to be noted: (1) a leucocytosis; (2) albuminuria with blood and epithelial casts: (3) post mortem toxic nephritis.

Histologically, in the stage of epithelial hypertrophy, the author describes loosening and separation of connective tissue, marked increase of mast-cells and elastic fibres at the periphery of the growth.

In the stage of downgrowth these reactions diminish and gradually vanish entirely, so that finally elastic fibres are demonstrable only in the capillary walls.

Put briefly, the invaded structure reacts only as long as the sharp demarcation between epithelium and connective tissue persists; thereafter co-ordination of resistance (*i. e.* epithelial and elastic hyperplasia) appears to give way, and the further progress of the invasion is unobstructed.

The first stage, viz. epithelial hypertrophy, can also be produced by arsenic, and it occurred to the experimenter to institute his tar applications in mice already under the influence of the former drug. It was then found that malignancy was delayed on an average to the 188th instead of the 131st day—a prolongation of the incubation time of about 50 per cent. Basing the results on thirty-two animals treated by the combination of arsenic and tar, it would thus seem possible to increase the resisting power of connective tissue against the advance of malignant epithelial cells.

H. S.

"CANCER OF THE SCROTUM": THE ÆTIOLOGY, CLINICAL FEATURES AND TREATMENT OF THE DISEASE. A. H. Southam and S. R. Wilson. (*Brit. Med. Journ.*, 1922, ii, pp. 971–973.)

These writers found that 141 cases of cancer of the scrotum had been admitted to the Manchester Royal Infirmary during the years 1902–1922. The average age of these patients was 51 years. The analysis of their occupations is of

considerable interest: Mule spinners, 69; tar and paraffin workers, 22; sweeps, 1; various occupations, 38; occupations not stated, 11. These figures show that epithelioma of the scrotum was largely associated, in South Lancashire, with two occupations—cotton-spinning and employment in tar and paraffin. Cotton-spinning is one of the chief industries in this district. The authors find that of this series of cases, 53 per cent. were engaged as mule spinners. In this area men only conduct this operation, and to the peculiarities of the work the writers attribute this large proportion of cases of scrotal cancer.

The "mule minder" has to piece together the ends of cotton thread, which are constantly breaking. To do this he has to reach over the moving "mule carriage." To this, about 3 ft. from the floor, is attached a steel bar. This rod is freely splashed with oil from the "oil-cups" in which the ends of the "spindles" revolve. Consequently, at this level of the body, his linen trousers and shirt, which are all he wears, become soaked with oil. This penetrates his clothing and bathes his scrotum and upper part of his thighs. As the man almost always leans over the "carriage" on his left side, the front part of the left scrotum is generally affected. The oil used for lubricating is mineral oil.

The writers consider that these cancers are caused by the friction of the clothes due to constantly pressing against the steel bar, added to the irritating effects of the oil.

The growth always begins as a solitary wart. If it is removed locally only, eighteen months later malignant deposits are likely to occur in the groin. In the above series of cases the testicle was involved six times and in three the disease spread to the penis. Usually there is little tendency to metastasis in distant organs. In this paper the authors describe at length the operation they consider necessary. In all cases, to be successful, it must be early and radical.

R. P. W.

MALIGNANT ENDOTHELIOMAS WITH CUTANEOUS INVOLVEMENT. George J. Busman. (*Arch. of Derm. and Syph.*, 1922, vi, p. 680.)

In this contribution three cases of tumours, which were believed to be malignant endotheliomata, are described. The tumours were of slow growth, and metastasis only occurred when they had reached considerable size. They all exhibited a marked tendency to hæmorrhage, and histologically presented the characteristics of a growth of endothelial cells. The cells were of an undifferentiated polymorphic type with a whorl arrangement, and the formation of elongated strands and narrow trabeculæ. A constant feature was the occurrence of vacuoles in the cytoplasm of practically all the cells. Capillary and sinus-like channels containing blood were also present, but these apparently had no connection with the general circulation.

The treatment consisted of surgical removal, followed by X-ray and radium applications to the site of the original lesion, and to all probable metastases.

J. M. H. M.

TREATMENT.

POTASSIUM PERMANGANATE AS A CURATIVE AGENT IN DERMATOLOGIC DISEASES. Samuel Feldman and Benjamin F. Ochs. (*Arch. of Derm. and Syph.*, 1922, vi, p. 163.)

The writer advocates strongly the use of solution of potassium permanganate for the cure of local skin affections, such as eczematoid ringworm and intertrigo.

They employ it in strengths ranging from 1 in 5000 to the full saturated solution, the former in early, moist and irritated lesions, the latter in those associated with deep infiltration and lichenification. The weak solution is used in the form of wet dressing, while the strong solution is painted on. J. M. H. M.

INTRA-CUTANEOUS INJECTIONS OF "LACTIN." Gawalowski. (*Ceská Dermatologie*, 1922, iii, p. 147.)

"Lactin," a milk preparation for intra-cutaneous injections, causes, like many other foreign proteins, an acute inflammatory reaction in chronically diseased areas, thus increasing their vitality. At the skin clinic in Prague "lactin" was used in sixteen cases of deep parasitic sycosis with good results. It might be of value especially to a country practitioner to whom X-rays and specific trichophytin are inaccessible.

0·2–0·5 c.c. doses were used to produce a local reaction. The dose was repeated after the first reaction subsided. Two to eight doses are necessary. Cases of chronic sycosis coccogenes were not benefited. Spinka (St. Louis).

SYPHILIS.

PRIMARY SCLEROSIS OF THE EYELID. Deyl. (*Ceská Dermatologie*, 1922, iii, p. 258.)

A young pregnant woman (five months) presented a painless, cartilaginous, purple-red induration of the right upper eyelid with papulo-squamous brownish-red lesions on the forehead, falling out of eyebrows and lashes. Wassermann ++++. Genital examination negative for lues. No traces of other primary luetic lesions on the body. The unusual features of this case are (1) the lack of a typical primary ulcer—the lesions on the eyelid involved without ulceration, and (2) the lack of submental or pre-auricular adenopathy; there were a few enlarged posterior cervical glands and one above the clavicle. The findings cleared up in 4 months under combined treatment. The patient gave birth to a healthy child. The article contains a detailed differential diagnosis, especially the exclusion of tarsitis syphilitica. Spinka (St. Louis).

PUNCTURE OF GLANDS AND ITS SIGNIFICANCE IN THE DIAGNOSIS OF SYPHILIS. V. Sedlak. (*Ceská Dermatologie*, 1922, iii, p. 201.)

Puncture of indurated glands resulted in the finding of spirochates in 50 out of 52 cases examined during the first stage, and in 18 out of 21 cases of the secondary stage. The puncture seems of a great diagnostic significance, especially in cases of chancres negative for spirochætes—treated or inaccessible (phimosis)—and while the Wassermann reaction is yet negative. A positive gland puncture may decide the diagnosis in time for abortive treatment.

Spinka (St. Louis).

EXPERIENCES WITH THE DOLD PRECIPITATION REACTION. M. Dzinban. (*Ceská Dermatologie*, 1922, iii, p. 273.)

The author used Dold's original technique on 600 cases and compared the results with those of Wassermann and Sachs-Georgi reactions. They ran parallel in 92·83 per cent. of cases; in 98·16 per cent. Dold and Sachs-Georgi agreed; Wassermann and Dold reactions agreed in 90 per cent. on early reading

and in 93·3 per cent. on late reading of precipitation. To shorten the time of the reaction the author in some cases centrifuged the serum and the antigen, which had been previously incubated from 1–2 hours. In strongly positive cases the results could be interpreted in 5–10–15 minutes. When results were doubtful the author added the complement and the hæmolytic system to settle the question, as according to Gaehtgens and Salvioli only specific precipitates hinder hæmolysis. SPINKA (St. Louis).

INTRAMUSCULAR INJECTIONS OF NOVARSENOBENZOL "GLUCO 914" IN THE TREATMENT OF SYPHILIS. A. MESKA. (*Ceská Dermatologie*, 1922, iii, p. 250.)

THIS preparation, put up by Robert and Carrier, Paris, is recommended for cases in which for some reason or other the intravenous injections cannot be used. The neo is dissolved in glucose and comes in convenient syringe ampoules ready for use. The method is simple and almost painless. Good results of treatment combined with mercury are reported. SPINKA (St. Louis).

THE PREVALENCE OF YAWS (FRAMBESIA TROPICA) IN THE UNITED STATES. HOWARD FOX. (*Arch. of Derm. and Syph.*, 1922, vi, p. 657.)

A CASE of yaws in a negress is here reported, and the question of the prevalence of the disease in the United States is discussed.

According to the writer, it is doubtful whether yaws occurred in the Southern States in the early days of slavery. At the present time it is a rare disease in the United States, in spite of its great prevalence in certain parts of the West Indies. The majority of recorded cases have been imported from foreign countries.

With the modern treatment with arsphenamin the disease could easily be eradicated if it ever obtained a foothold in the Southern States.

J. M. H. M.

BOOKS RECEIVED.

Diseases of the Skin. By R. W. MACKENNA, M.A., M.D., B.Ch., Hon. Dermatologist to Royal Infirmary, Liverpool. 1923. Royal 8vo. Pp. x + 460. 160 illustrations. London: BAILLIÈRE, TINDALL & COX. Price 21*s.* net.

Frambœsia Tropica. By R. L. SPITTEL, F.R.C.S., Surgeon to General Hospital, Colombo. 1923. Demy 8vo. Pp. iv + 59. 39 illustrations. London: BAILLIÈRE, TINDALL & COX. Price 5*s.* net.

X-Ray Dosage in Treatment and Radiography. By W. D. WITHERBEE, M.D., and J. REMER, M.D. 1922. New York: THE MACMILLAN CO. Price 8*s.* net.

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THE PATHOGENESIS OF XANTHOMATOSIS, WITH REPORT OF A CASE.

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AND

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Considerable interest has been evinced in this comparatively rare disease during recent years, largely we believe on account of the introduction into clinical medicine of relatively simple methods of blood analysis. The following case has been fairly thoroughly investigated on modern lines, and is of especial value in that it would appear to occupy an intermediate position between the types with frank diabetes and the varieties without any glycosuria.

Mrs. W—, aged 62 years. Small lumps were noticed on both elbows twelve years ago, at the end of the climacteric. The patient states that her arms became excessively freckled at the same time, and that between the ages of 45 and 55 she gained 3 st. in weight. She was seen by one of us (A. W.) in 1913, and exhibited before the Dermatological Section of the Royal Society of Medicine (Whitfield [22]). The nodules on the left elbow disappeared after a single application of carbon dioxide snow in October, 1913. Those on the right elbow were treated with X-rays—three or four applications with intervals of three weeks—later in 1913 without effect. In 1915 or 1916 one of the nodules on the right elbow was frozen. The patient did not return for treatment until 1922 when she noted that the elbows were a little tender on rising from bed. In May this year two more nodules were successfully treated with carbon dioxide snow. In August a large nodule was excised for histological and

* Working on diabetes with a grant from the Medical Research Council.

chemical examination. There now (October, 1922) remain three nodules the size of a pin's head on the right elbow and several superficial scars. There are no xanthoma lesions elsewhere, nor have there been at any time.

In the past the patient has been singularly free from disease. She cannot remember having suffered from any serious complaint either as a child or in adult life. She has been in the habit of taking two glasses of stout daily and frequently a glass of whisky at night. She states she is fond of potatoes and sugar.

She comes from a long-lived family. Her father died at 97. Her mother was stout in her later years (she weighed 13 st.), and one of her sisters was a little obese. Her mother's sister died of cancer of the breast. There is no history of diabetes, of xanthomatosis, or of tuberculosis in the family. The patient is married and has two children. There is no history of a miscarriage.

She is obese and weighs 194 lb. in her clothes. Her height is 5 ft. 8 in. The average weight for this height, at the age of 40 and over, is 161 lb. On examination nothing abnormal has been detected in her chest or abdomen. Clinically the ductless glands appear normal. A skiagram of the pituitary fossa reveals nothing abnormal. She has one carious and eighteen normal teeth, and wears an upper and lower denture. There is no pyorrhœa, and no foci of sepsis have been located. The radial artery is not thickened. The systolic blood-pressure is 115, and the diastolic 80 mm. Hg. The knee-jerks are brisk and no abnormality has been found in the nervous system. A blood-count was made on August 4th, 1922: Erythrocytes, 5,064,000; no abnormal forms seen. Hæmoglobin, 92 per cent.; colour index, 0·91. Leucocytes, 6800, of which polymorphonuclears constituted 71·6: eosinophils, 2·0; lymphocytes, 25·6; and hyalines, 0·8 per cent. The patient bruises easily, but her flesh heals very rapidly and completely. The fragility of her red blood-corpuscles has been measured by Dr. E. ff. Creed, who kindly allows us to report his results: "There is a trace of hæmolysis in 0·44 per cent., and hæmolysis is almost complete in 0·36 per cent. sodium chloride" (a typically normal result). The Wassermann reaction is negative.

Examination of the urine.—The output in 24 hours was 80 oz. (9 . 8 . 22), the specimen being acid to litmus and having a specific gravity of 1015. In 1913 one of us (A. W.) found the urine to be free from sugar and albumen. In May, 1922, there was no glycosuria on her ordinary diet, but a trace of glucose was excreted after oral administration of 50 grm. In August four out of five specimens were free from sugar. The fifth contained a very slight trace of a reducing substance which was fermented by yeast. Ketonuria, urobilinuria and indicanuria were consistently absent. There was no albumen in a specimen obtained by catheter. Microscopical examination of the centrifugalised deposit revealed nothing abnormal.

Pancreatic and hepatic function.—Loewi's adrenalin mydriasis test was negative. Reference has been made to the very occasional glycosuria. The diastase content of blood and urine was normal; plasma diastase, 3 units; urinary diastase (reaction of urine adjusted to pH 6·7), 6·7 units; volume of urine 2272 c.c.; total excretion of diastase in 24 hours, 15,200 units. The fæces were pale and semi-liquid, but there was no steatorrhœa. On microscopical examination (no purgatives had been taken and no other stool was passed in the 24 hours) there was a marked excess of undigested muscle-fibres. Of these, many showed evidence of partial digestion—either loss of striations, or striations visible but ends rounded—

while a large number showed perfect striation and quite irregular ends. Creatorrhœa was therefore present. Neither fatty acid crystals nor fat-globules were seen under the microscope.

Chemical examination yielded the following figures:

Neutral unsplit fat . . . . . 12·0 } Total fat = 13·9 per
Split fat (fatty acids, free and combined) 1·9 } cent. of dried fæces.

Though the total fat is within normal limits, the amount of unsplit fat is high, the normal figure being 1 to 2 per cent. Stercobilin was present. There was no jaundice, and Van den Bergh's test for bilirubin in the blood plasma was normal—0·2 units. As already mentioned there was never any urobilinuria. On May 5th, 1922, the blood-sugar was 0·14 per cent. 2½ hours after a mixed meal. On May 25th the blood-sugar was estimated before, and at half-hourly intervals after, the administration of 50 grm. of lævulose. Later in the day a similar procedure was adopted using 50 grm. of dextrose. The estimations were made by MacLean's method (see Cole [9]). The urine was examined hourly for sugar (Benedict's test) and for lævulose (Seliwanoff's test). The results are given in Table I, and in the chart. For comparison, normal blood-sugar curves are given in dotted lines. The normal lævulose curve is taken from a paper by Spence & Brett (*Lancet*, 1921, ii, p. 1364), and the normal glucose curve is the average of Spence's results in five old men (*Quart. Journ. Med.*, 1921, xiv, p. 314.)

Table I.

Time.	Blood-sugar per cent.	Urine.		
		Volume c.c.	Sugar. (Benedict's test.)	Lævulose. (Seliwanoff's test.)
6.0 a.m.	½ pint of	milk.		
10.25 „	0·16	—	0	0
10.30 „	50 grm. of	lævulose	in 200 c.c water by	mouth.
11.0 „	0·18	—	—	—
11.30 „	0·19	25	Trace	Trace
12.0 noon	0·17	—	—	—
12.30 p.m.	0·16	20	Trace	Trace
12.45 „	50 grm. of	dextrose	in 200 c.c. water by	mouth.
1.15 „	0·21	—	—	—
1.45 „	0·195	19	Trace	Slight trace
2.15 „	0·19	—	—	—
2 45 „	0.15	15	Slight trace	Very slight trace
5.15 „	—	40	Very slight trace	0

Cholesterolæmia.—The first of the three estimations was made on whole blood by the method of Autenrieth and Funk, and the last two on plasma using Bloor's procedure. The patient was on her usual unrestricted diet on each occasion.

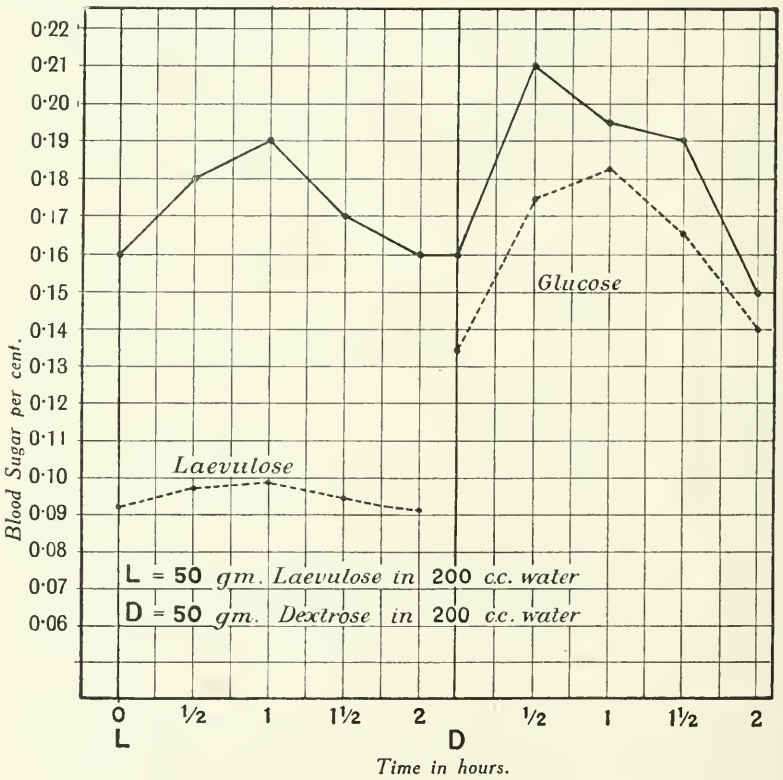
Date.	Blood cholesterol. mgrm. per 100 c.c.	Time of blood collection. Hours after last meal.
5 . 5 . 22 . .	325 . .	2½
4 . 8 . 23 . .	610 . .	4½
17 . 10 . 22 . .	613 . .	1¾

Lipæmia was very marked, the fresh plasma being extremely milky in each instance.

Renal function.—Catheter specimens were free from protein, and microscopically the centrifugalised deposits showed nothing abnormal. There was no diastase retention (see last paragraph but one). The urea concentration test (MacLean and de Wesselow—dose 15 grm. by mouth) gave the following:

	Urea per cent.	Urea c.c.
At end of first hour	2·16	85
„ second hour	2·30	100
„ third hour	2·41	60

The blood urea, $2\frac{1}{2}$ hours after the above dose, was 64 mgrm. per 100 c.c. of blood, and the urea concentration factor (third hour of urea concentration test —Harrison [12]) was 38. The blood urea on her ordinary diet (no urea by mouth) was 40 mgrm. per 100 c.c. of blood. In short, no evidence was obtained of renal damage.



Report on Biopsy. (*a*) Microscopical (A. W.).

The tissue examined consisted of a piece of skin containing a nodule rather less than an eighth of an inch in diameter lying in the corium.

The tissue was fixed in the formalin and cut by means of the freezing microtome.

Sections were stained—(*a*) first with Sudan III for variable periods so as to

obtain different densities of stain, and subsequently with hæmatoxylin. These were mounted in glycerin jelly. (*b*) After passing through alcohol, first with hæmatoxylin and then with orange rubin mixture. (*c*) After passing through alcohol, first with hæmatoxylin and then with picric acid fuchsin by Hansen's method.

Taking first the ordinary histological structure, it is at once seen that the nodule is very definitely circumscribed and bounded by coarse strands of fibrous tissue arranged concentrically around it.

The nodule itself consists of a very cellular fibrous tissue disposed somewhat regularly and concentrically in small areas, so that it seems to be composed of several foci bound together by a capsule.

The very numerous cells of the nodule may be divided into three classes:

(1) Very long spindle-shaped cells with long oval nuclei, poor in chromatin. These are evidently immature fibroblastic cells, such as one sees in any organising granulation-tissue.

(2) Small lymphoid cells with a round or indented nucleus rich in chromatin. This is the type familiar in all chronic inflammatory reactions, and commonly called the "small round cell."

(3) Large cells of variable character, but evidently belonging to one group. These cells have an abundant protoplasm and vary greatly in size. Most are of about three times the diameter of a lymphoid cell and roughly circular in outline. Many are, however, oval with nucleus driven to one end, and some few are irregular and large enough to be called giant cells. The cytoplasm shows, in those sections which have passed through xylol a foam-like structure with vacuoles of various sizes. The nuclei are rich in chromatin and are in different cells, either simple or lobed, or in the very large cells multiple, but there are present none of the striking giant cells with a complete ring of nuclei such as are often seen in xanthoma nodules.

In the sections stained with Sudan III red droplets are seen in such abundance as to obscure the structure of the tissue. Where, however, the staining has not been effected too deeply, it can be clearly made out that the vast majority of the droplets are contained in the protoplasm of cells of the classes (1) and (3). There are numerous small droplets which cannot be connected certainly with cell protoplasm, but as these are always arranged in rows, and generally in tapering rows, it is probable that they lie in pieces of the protoplasm of cells of class (1) cut off by the microtome knife.

No crystals were observed after a prolonged search. On examination with the polariscope many of the droplets were seen to be anisotropic.

The tissue surrounding the nodule is evidently in a state of abnormal activity. Most of the vessels show accumulations of clasping cells and some proliferation of the endothelium. It is especially noteworthy that many of these cellular foci, well away from the main xanthomatous lesion, show the sudanophilous droplets in the endothelium and the clasping cells.

(*b*) Chemical (G. A. H.).

A small portion of the nodule was teased out in water and examined microscopically. No cholesterol crystals were seen. The major part of the lump was separated from neighbouring tissue and was cut into minute pieces. These were extracted with an alcohol-ether mixture on the water-bath. The extract was

evaporated just to dryness, and the residue taken up with a few c.c. of chloroform, as in Bloor's method for estimating blood cholesterol. To one portion of the chloroform extract 2 c.c. acetic anhydride and 0·1 c.c. sulphuric acid were added. An intense blue colour developed immediately. The other portion of the chloroform extract was evaporated on the water-bath, and then dissolved in a minimum of hot alcohol, cooled, and examined microscopically. The alcohol was allowed to evaporate, the specimen was mounted in water, and again examined. A number of acicular crystals but no cholesterol crystals were seen. It is concluded that the nodule contained a large amount of cholesterol ester, but none of the free substance.

Discussion.

Whitfield ([23]) has recently reviewed the relation of cholesterolæmia to xanthomatosis. Nearly all observers have found an increase in the blood cholesterol. The present case shows a marked hypercholesterolæmia. Rosenbloom ([16]), and Rosenthal and Braunisch ([17]), however, found values well within normal limits. The former used the digitonin method, but the latter employed the colorimetric procedure (Autenrieth and Funk). The choice of methods therefore is probably not responsible for the relatively low figures. To quote Whitfield ([23]), " . . . it is now generally believed that the tumour-like growths are due to the irritation of the tissues by the deposit of cholesterol in them. At the discussion on Dr. Burn's paper ([5]), it was pointed out that xanthoma-like masses had been produced by feeding rabbits with cholesterol, and then inflicting local injury to determine the site of deposit" (Anitschkow ([1])). The xanthoma-like masses were shown to contain cholesterol, but we have not discovered any records of estimations of blood cholesterol in these experimental animals. Chauffard and Laroche ([7]), in their original paper, report four cases of xanthoma in which cholesterol estimations were made. In two there was hypercholesterolæmia, but in the other two the values were within normal limits. The authors suggests that one of the latter results was probably due to the long duration of the condition, whilst the other might be explained by the presence of tuberculosis (renal), which tends to produce hypocholesterolæmia. Similarly, subsequent workers have generally considered that the occasional finding of a normal cholesterol content is due to persistence of the xanthoma lesions after the hypercholesterolæmia has disappeared.

Rosenthal and Braunisch ([17]), however, suggest that xanthoma nodules may result from a local formation of cholesterol esters following injury to, or degeneration of, cells at the particular site. If the

primary damaging noxa also injures the cholesterol-excretory function of the liver, then an excess of cholesterol in the blood will follow, but hypercholesterolæmia is not essential for xanthomatosis. (In a similar manner they would explain the various findings associated with xanthomatosis as due to a common toxin affecting the different organs.) In favour of such a view is the fact that in diabetes mellitus hypercholesterolæmia is relatively common whereas xanthoma deposits are distinctly uncommon. Schmidt ([18]) finds that extirpation of xanthoma nodules does not alter the percentage of cholesterol in the blood, for which reason he concludes that the process is one of infiltration, and not of degeneration. This does not follow, however, for on Rosenthal and Braunisch's hypothesis he has merely removed a cutaneous lesion without influencing the more general effect of the toxin on the glands controlling fat metabolism.

The following summary (Table II, see p. 88) of the cholesterol content of the blood in xanthomatosis is taken from the literature at our disposal.

The second point to which Whitfield ([23]) alludes is the presence of a pancreatic lesion in xanthomatosis. In the case reported in this paper there is definite evidence in favour of pancreatic disease, viz. a diminished power to deal with absorbed glucose and fructose, very occasional mild glycosuria, a glucose tolerance of less than 50 grm.; hypercholesterolæmia, lipæmia, an excess of unsplit fat in the fæces, and creatorrhea—evidence which indicates an abnormality of both internal and external secretions. At the same time it is noteworthy that the patient has had xanthoma for twelve years, and that clinically she is, and always has been, an extremely healthy woman. It is possible that hypercholesterolæmia must exist for a long time before xanthoma deposits occur. This would account for the comparative infrequence of xanthoma in diabetics with hypercholesterolæmia. Excess of blood cholesterol is usually regarded as a bad omen in diabetes, but it responds rapidly to suitable dietetic treatment, and is more probably merely a symptom of a high fat diet, which is now generally recognised as dangerous. It is possible, therefore, that on the contrary xanthoma in diabetes is a good prognostic sign, implying that the disorder of fat metabolism is of long duration and that the diabetes is inherently mild. Such, at any rate, would appear to have been the situation in the recent case reported by Lyon ([14]).

TABLE II.—*Cholesterolæmia in Xanthomatosis.*

Author.	Year of publication.	Type of xanthoma.	Serum cholesterol mgrm. per 100 c.c.	Method of cholesterol estimation.	Remarks.
Chauffard et Laroche (7)	1910	1. Palpebrarum	190	Grigaut I.	Normal values by this method 10–40 mgrm. per 100 c.c. serum.
		2. „	60	„	
		3. „	12	„	
		4. Not stated	10	„	
Thibierge et Weissenbach (20)	1911	Multiplex	575	Grigaut II	Average normal 180.
Chvostek (8) .	1911	Multiplex	265	Windhaus	Average normal 175.
Autenrieth und Funk (3)	1913	Tuberosum	580	Autenrieth und Funk	Normal 140–180.
Rosenbloom (16)	1913	Multiplex	70	Windhaus	Normal control 74.
Schmidt (18) .	1914	1. Tuberosum	575	Autenrieth und Funk	—
		2. „	259	Ditto	
		3. „	363	„	
		4. Palpebrarum	318	„	
		5. Tuberosum	414	„	
Alert . .	1918	Tuberosum	550	—	Quoted by Arning und Lippmann (2).
Hoffmann (13) .	1918	1. Diabeticorum	*a.* 2500 *b.* 330	Autenrieth und Funk	*b.* Estimation shortly before death.
		2. Diabeticorum	*a.* 2500 *b.* 477 *c.* 8·5	*a.* Ditto *b.* Digitonin *c.* Not stated	2. Prof. Mannheim's case. *c.* Blood obtained post-mortem.
Fahr (11) . .	1920	Diabeticorum	1404	Not stated	Blood obtained post-mortem.
Queyrat et Laroche (15)	1920	Multiplex	215	„	—
Spillmann et Watrin (19)	1920	„	525	Grigaut II	—
Arning und Lippmann (2)	1920	1. Multiplex	760	Autenrieth und Funk	Nos. 2 to 10 were women at the menopause. No 10 had latent diabetes.
		2. Palpebrarum	100	Ditto	
		3. „	160	„	
		4. „	120	„	
		5. „	200	„	
		6. „	220	„	
		7. „	340	„	
		8. „	240	„	
		9. „	420	„	
		10. „	440	„	
Burns (5) . .	1920	Multiplex	*a.* 650 *b.* 660 *c.* 999	Bloor	Normal (Bloor) 190–250. *a.*, *b.*, *c.*, normal, low and high fat diet. Gouty lesions on hands and feet.
Rosenthal und Braunisch (17)	1921	„	*a.* 140 *b.* 140 *c.* 130	Autenrieth und Funk	*a.*, *b.*, *c.*, three estimations on different dates.
Vas Nunes (21)	1921	„	486	Windhaus	—
Crozer Griffith (10)	1922	Tuberosum	397	Not stated	Jaundice and diabetes insipidus.

Cases have been published by several authors which show little or no evidence of pancreatic disease in spite of chemical investigations. Thus Arning and Lippmann ([2]) obtained a normal blood-sugar curve after 100 grm. of dextrose, and Rosenthal and Braunisch ([17]) found no sugar in the urine after 100 grm. of dextrose, after 100 grm. of lævulose and after 40 grm. of galactose. At the same time, except in xanthoma with frank diabetes, so far as we are aware, pancreatic function tests have not been applied as fully as in the present instance. The possibility remains therefore that most, if not all, cases of xanthoma would show evidence of pancreatic disorder of varying degree if sought for carefully. One of us (A. W.) clinically had not regarded Mrs. W—, as in any sense a diabetic. The other (G. A. H.) estimated her blood-sugar at the same time as her blood-cholesterol because she was stout, and owing to the slight hyperglycæmia carried out the tests detailed above. "There are . . . dissenters who claim a 'lipogenetic' origin of diabetes, basing their claim on the frequent occurrence of obesity preceding diabetes, and the occasional clinical observation that the rapid laying on of fat is accompanied by glycosuria, which disappears when the fattening process is stopped" (Bloor ([1])). It may be that in the lowest grade of pancreatic insufficiency there is a slight error in fat metabolism; later a disorder of total metabolism; a prediabetic condition; and finally the various grades of diabetes mellitus. On this view Mrs. W— may be said to be in the prediabetic state. It would be interesting to test the effect of "insulin" on her hyperglycæmia and lipæmia.

Several investigators have considered xanthoma to be due to a failure of the liver to excrete cholesterol. But the error is not confined to cholesterol metabolism. Thus Burns ([5]) showed in his case that there was also a piling up of fat in the blood, and Arning and Lippmann ([2]) showed in their patient that not only cholesterol but also neutral fat and lecithin were increased. It would be interesting to estimate the cholesterol content of the bile removed by duodenal tube. Rosenthal and Braunisch ([17]) did perform this test on their patient and found no diminution in cholesterol excretion, but they also found no hypercholesterolæmia.

No doubt the chief reasons for referring the condition to hepatic insufficiency are the association with jaundice and the raised blood uric acid reported in some cases. Chauffard and Laroche ([7]),

estimated the cholesterol content of the blood in eight patients with icterus. Hypercholesterolæmia was present in all, but they noted that the two conditions were relatively independent. Thus the highest cholesterol content was found in a patient with merely a subicteric tint. They further applied Liebermann's reaction for cholesterol to the skin obtained by biopsy from the face and arm of fourteen cases with jaundice, and found five positive and nine negative as compared with five normal individuals similarly tested. They therefore postulated a "prexanthelasmic state." They regard xanthomatosis as analogous to gout and Chauffard ([6]) and others have found large amounts of cholesterol ester in gouty tophi. All this at first sight appears strongly in favour of a hepatic origin for xanthomatosis. But disease of the liver or its passages is frequently accompanied by disease of the pancreas, and Chauffard and Laroche ([7]) themselves feel it unnecessary to separate xanthoma diabeticorum from the other clinical types, and prefer to conclude that xanthoma is due to hypercholesterolæmia—an abnormal metabolism of fats, probably the result of a lipolytic insufficiency of the pancreas. In some cases the jaundice has been ascribed (Crozer Griffith ([10])), to a mechanical blocking of the bile-passages by xanthomatous deposits. It would be valuable in such cases to apply Van den Bergh's test, in the hope of deciding whether the jaundice was obstructive or otherwise. It is not easy to devise methods for testing the function of the liver to the exclusion of the pancreas in man. An abnormal response to the lævulose test for instance may be due to disease of either organ. In the case here reported the fæcal examinations definitely favour a pancreatic lesion.

In conclusion it would seem to us, after consideration of the above data, (1) that xanthomatosis is probably a process of infiltration dependent primarily upon hypercholesterolæmia, and secondly upon the duration of the blood condition, local trauma, local vascular supply, etc., and (2) that such hypercholesterolæmia is part of a disturbance of fat metabolism resulting probably from pancreatic disease.

Note by A. W.—Accepting the evidence of pancreatic insufficiency, an alternative conclusion seems to me equally if not more likely. I would suggest that the pathogenesis of the xanthoma lesion in our patient is somewhat as follows:

Owing to the erroneous tissue metabolism caused by the deficiency of the internal secretion of the pancreas, the cells of the body in the natural course of their senescence and death do not go through the ordinary cycle of chemical changes which occur in the normal individual. The process is either altered in character or arrested before the chemical change is complete enough for absorption and carrying away to take place. This alteration or arrest leads to the deposit of a cholesterin ester which is carried away only with difficulty. In parts where death and absorption naturally take place in excess of the normal, *i. e.* where a temporary newly formed aggregation of cells occurs after slight irritation or inflammation, this leads to the more or less permanent deposit of the cholesterol ester.

If this idea be correct the first change in the tissue is probably the result of a slight trauma or infection, which causes an infiltration of fibroblastic cells. In the normal course of events these cells, having served their purpose, are absorbed and disappear entirely, but in the xanthomatous patient they lead, owing to the arrest of chemical changes, to the local deposit of the cholesterol ester.

Where cells such as leucocytes undergo death in the glands and circulation the cholesterol ester will appear in the blood. In the less vascular tissues, such as the fibrous tissue, the deposit will remain unabsorbed in the tissue.

This theory would, therefore, account for the presence of the hypercholesterolæmia, and the cholesterol ester in the tissues.

On the other hand, if the hypercholesterolæmia were the prime cause of the local deposit, one would expect to find the deposit most marked in the centre of the nodule, but this is not the case, since the sudanophilous substance is equally dense in the long fibroblastic cells at the extreme periphery of the nodule. Also it is to be remembered that the sudanophilous substance is found in many, though not in all, of the aggregations of proliferated perivascular cells well away from the xanthomatous nodule itself, and this suggests that wherever masses of cells degenerate the xanthomatous deposit occurs.

Summary.

A case of xanthoma tuberosum, which clinically showed no evidence of diabetes, has been investigated by modern pathological methods.

The evidence points to the existence of a pancreatic lesion in this

case. The presence of hepatic insufficiency is regarded as unlikely. Renal inefficiency is excluded.

The main points in the pathogenesis of xanthomatosis are discussed.

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CARBON-ARC LIGHT BATHS IN THE TREATMENT OF LUPUS VULGARIS.

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The value of the local application of concentrated light in the treatment of lupus vulgaris introduced by Finsen is incontestable, but those who have had experience of this therapeutic measure have long recognised that a certain type of case has a tendency to increase too rapidly to be dealt with adequately by this local measure, or, if apparently cured, is likely to relapse. In reports which I have made from time to time on the work of the Finsen Light Department at the London Hospital ([1, 2]) I divided my patients into classes:

Class A.—Permanent cures—about 70 per cent.

Class B.—Cases temporarily cured which require occasional treatment for recurrences of small dimensions. The majority of these patients are able to follow their employment, and, as a rule, respond rapidly to treatment, and after a few sittings are able to resume their work—about 11 per cent.

Class C.—Those who benefit by this treatment but have never been freed from evidence of disease. In many of these there is extensive lupus of the nasal cavity, and in others the area affected is so large that it is impossible to eradicate the whole of the disease—about 16 per cent.

The remainder, about 3 per cent., are cases which are quite intractable.

The permanence of the cure in Class A was recently tested by a circular letter to patients who had been placed in this group in 1913. As ten years had elapsed, we failed, of course, to trace a large number of patients owing to the war, removals, marriage, etc., but we got into touch with 132 who had been treated prior to 1913, and these were either personally examined, or we obtained satisfactory evidence that the cures effected from ten to

twenty-two years ago had been permanent, and this in spite of the failure of nutrition due to war conditions.

In Class B there were, of course, slight relapses, and most of these had been dealt with in the department. Some of them were ultimately cured and could be placed in Class A.

Our experience in the London Clinic almost coincides with that of Reyn, who stated that of the collected material from the Finsen Light Institute at Copenhagen the percentage of cures from the local application of light is over 60 per cent., and from our personal experience of the Copenhagen Clinic we believe that a graver type of lupus than we see in London gravitated there, especially in the earlier years of its work. Reyn, however, has for some time been using light baths in addition to the use of concentrated light locally, and he claims that the percentage of cures can be raised to 90 per cent. if both measures are employed simultaneously. (Quoted by Heiberg and With [5].)

Strandberg and Heiberg [3, 4], working in the Finsen Institute, have shown that light baths without any local treatment will heal intranasal lupus, and Heiberg and With recently published a paper in the *British Journal of Dermatology* [5] on the treatment of lupus with carbon-arc light baths alone.

The cure of surgical tuberculosis by sun baths has been amply demonstrated by Rollier at Leysin, and Gauvain at Alton and Hayling, and it is clear from the experience of the latter that these effects are due to light and not to a high altitude. There seems to be no doubt about the efficacy of the treatment being in direct proportion to the intensity of the pigmentation.

Last summer I decided to try the effect of exposing cases of lupus which failed to be influenced by the local application of concentrated light to light baths, and in August a 25-ampère lamp was installed in my department for this purpose. As immediate improvement was observed, I got the authorities to put in a larger (50-ampère) arc lamp, and thus could treat more patients with better effect. The carbon-arc light is placed about three feet from the ground; the patients, clad only in bathing drawers, are seated around this. The whole of the body and the limbs are exposed to the light of the arc, care being taken to protect the eyes by thick shields when the anterior surface is under treatment. My colleague, Mr. Goulden,

kindly inspected and passed the protection of the eyes as adequate. At first the sittings are of half an hour's duration, and they are gradually extended until both anterior and posterior surfaces are exposed for two hours. Any open sores are covered by a simple

The carbon-arc light bath at the London Hospital.

dressing. The sittings are given daily. The group of nude figures round the lamp is surrounded by a screen, and care is taken to prevent the possibility of the blind-folded patient coming too near the arc.

We are now treating eight at one arc lamp at once. So far we have only given the light-bath treatment to cases of lupus which

have failed to respond adequately to the local application of light. The effects observed are:

(1) Intense pigmentation of whole surface.

(2) Rapid healing, especially of moist rather fungating lesions.

(3) Increase of body-weight.

(4) Improvement in the general condition. Listless, apathetic lads become bright and keen on their cures.

(5) In some instances an increase of the lymphocytes in the blood-count.

We hope in the near future to investigate the basal metabolism

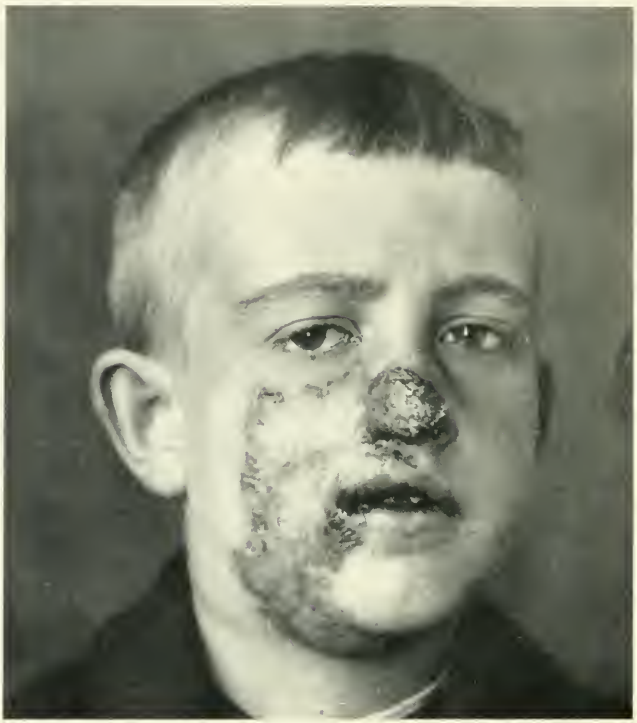

Fig. 1.—September 10th, 1921: Before Finsen treatment.

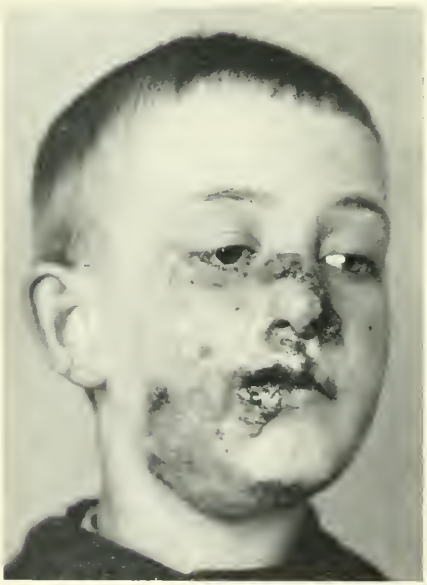

Fig. 2.—May 7th, 1922: After Finsen treatment. Large area cicatrised, but lupus extending at margins.

Fig. 3.—January 30th, 1923: After 5 months' light-bath therapy with no local treatment.

TO ILLUSTRATE DR. SEQUEIRA'S ARTICLE ON CARBON-ARC LIGHT BATHS IN THE TREATMENT OF LUPUS VULGARIS.

and other factors of biological interest, and also to try the effect of the treatment on other conditions.

I illustrate here a characteristic case shown with another at the Dermatological Section in January. The boy, whose photographs are appended, came under treatment in September, 1921. He was treated by the local application of concentrated light until May, 1922, and although parts of the affected area healed under this measure the disease spread at the periphery (Figs. 1 and 2). He was then submitted to the light bath only, local treatment being suspended, and in the third photograph the improvement is obvious. We shall now combine both therapeutic measures to finish the few remaining nodules. In another case shown, not only had the lupus healed but an old sinus of the shoulder closed completely.

Carbon-arc light is preferred by Reyn after experimenting with other forms of illumination and on several grounds this appears to be the best illuminant :

(1) The spectrum of the carbon-arc more nearly approaches the spectrum of sunlight.

(2) There is no need to have the light enclosed in an envelope of uviol glass or rock crystal.

I have gone into the cost of the outfit, and Mr. Delerset, electrician at the London Hospital, has supplied me with the following particulars :

The cost of the installation will vary with the current available.

If 100–110 volts direct current is employed the installation of a 20–25-ampère lamp would cost £35, a 50-ampère lamp £40.

If, however, a 200–240-volt direct current is available the installation of a 20–25-ampère lamp with motor generator would be about £100.

If instead of a motor generator a resistance be employed the installation would be under £50.

The electrician, however, points out that if the motor generator is used the consumption of current would be 1·4 units per hour, but with a resistance 4·8 units, there being a wastage of 180 volts and 20 ampères in heat. Moreover, there is a risk of shocks. If, however, the current from the main supply is 100–110 volts no motor generator would be required.

For a 50-ampère lamp the installation with motor generator would cost about £160.

At the London Hospital we already had motor generators installed and worked off the supply for the ordinary Finsen lamps.

In commending this measure to the notice of dermatologists and others I would point out that the Danish Government is so satisfied with its efficacy that they pay for the maintenance of patients while under treatment.

I desire to express my grateful appreciation of the assistance given me in carrying out this work by Dr. W. J. O'Donovan.

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MANGANESE AS A CHEMO-THERAPEUTIC AGENT.*

J. E. R. McDONAGH, F.R.C.S.

My early work with metallic chemo-therapeutic agents led me to believe that they act as oxidising agents so far as the host's protective substance in the form of the protein particles in the plasma is concerned. Consequently my attention was drawn to manganese and iron, two of the most suitable oxidising metals, because both can exist in two hydroxide forms which are readily reversible by hydrogen. The di-valent hydroxide appears to be the catalytic form, and in the oxidase reaction this is converted into the tri-valent hydroxide, which is changed again into the di-valent form by hydrogen. The hydrogen results from the reducase reaction which is executed by sulphur in its catalytic di-sulphide form. This led me to introduce a thio-compound of benzene as an aid to the treatment of syphilis by metals and as a

* Read before the Section of Dermatology of the Royal Society of Medicine, January 18th, 1923.

specific for metallic intoxication. This sulphur body has recently been replaced by the carbon di-sulphide compound of di-ethyl-amine under the name of contramine. Contramine is more efficient than intramine, it is soluble in water, and is painless when injected intramuscularly. As arsenic is a toxic metal and its oxidising power is less than that of manganese, I attempted to prepare a substance having a large molecule of which manganese was an integral part, and failed. I could get no further than the colloidal manganese hydroxide. One of the first successes gained with colloidal manganese was the rapid healing of the burns in cases of mustard-gas poisoning. Yperitis is due in my opinion to the sulphur fraction of di-chlor-ethyl-sulphide. Therefore finding that manganese caused the symptoms to vanish in like manner to those of arsenical dermatitis under the action of sulphur, the important information was gained that a metal is an antidote for non-metallic intoxication and *vice versâ*. About this time I was trying several of the colloidal hydroxides in syphilis, and found that those of bismuth, thorium and lanthanum rapidly cause the lesions to heal up, but that the hydroxide of manganese is of no value. In coccogenic infections the position is reversed ; manganese acts like a charm, while the other metals tend to aggravate the lesions. This led me to conclude that micro-organisms can be graded, the simplest one, the staphylococcus, causing the least change in the host's protective substance, and the highest one, the *Leucocytozoon syphilidis*, the greatest change. Further, that while highly complex metallic compounds are required in the latter, the opposite is the case in the former.

Owing to the great advances science has made since 1917, when colloidal manganese was first introduced, the action of chemo-therapeutic agents upon the protein particles can be described more accurately. Metallic preparations act as conductors of electricity and non-metallic preparations as condensers. All micro-organisms on gaining a foothold on the host behave as condensers. They rob the protein particles of some of their negative electricity, with the result that the latter increase in size and agglutinate. The degree of condensation the protective substance undergoes naturally depends upon the nature of the parasite. Staphylococci are among the feeblest condensers and the syphilitic organism among the most powerful. The degree of condenser action of a parasite can be

gauged by the length of time an aqueous solution of contramine takes to convert its Gram-negative property into Gram-positive. Gram-negative micro-organisms are stronger condensers than Gram-positive, and this explains why the former partially decolourise most of the tri-phenyl-methane dyes and why they are so readily able to enter the cells of the host. The greater the condenser action of the parasite, the more the surface tension is diminished. Conductors set free electrons, and these, when they reach those of the protein particles, cause a repulsion which, if sufficiently great, results in the atoms breaking up. When the atoms of the protein particles break up the particles become smaller, more negatively charged, more actively motile (Brownian movement), and present a greater expanse of surface. These changes are covered by the term "dispersion." When the particles become dispersed the tables are turned upon the parasites, and it depends upon how far the negative charge of the protective substance is increased as to whether the parasites are rendered merely dormant or are annihilated. Dispersion, if continued beyond its acme, results either in true solution or in condensation. In both cases the protective substance is diminished, consequently if the dose of the conductor employed is too great or is repeated too often, the parasites may be stimulated to renewed vigour. Herein lies the danger of chemotherapy. The best rough-and-ready means of determining the degrees of dispersion and condensation sustained by the protein particles is to measure the velocity with which the red blood-corpuscles fall in the citrated plasma. When the protein particles undergo condensation the red blood-corpuscles suffer the same change and agglutinate, the effect of which is to reduce their suspension stability and *vice versâ*.

Experience with colloidal manganese hydroxide in boils, carbuncles, etc., shows that the maximum degree of dispersion is attained with two, or at the most three injections, and that any number over this amount is apt to re-activate the lesions. This is the reason why opinions regarding the value of this drug vary; they do vary because the literature circulated with the preparation gives the wrong advice. While studying the effect metallic and non-metallic substances exert upon the blood, I found those metals which are good conductors of electricity accelerate coagulation, while non-metals retard it, and that metals which have a high atomic weight retard

coagulation, because the high atomic weight imparts to the metal an initial condenser action. As a result of my investigation into the *modus operandi* of coagulation, I came to the conclusion that the phenomenon is primarily dependent upon the number of the protein particles in the plasma, and that when blood is withdrawn the requisite number is formed by the protein particles dissipating some of their electrons and breaking up their atoms. This change occurs only when the blood comes in contact with a substance which is electrically active like glass. If the glass is lined with paraffin—an inert substance, hence its name, from *parum affinitatis*—the blood does not coagulate. I tested the action of a very large number of preparations upon citrated plasma, and found that acceleration of coagulation runs parallel with conduction and retardation with condensation. So far as the compounds of manganese were concerned, I found that the fatty acid preparations are the most efficient accelerators of coagulation, and that the best of them clot a citrated plasma as rapidly as do compounds of calcium and strontium. Most of the work was done with four fatty acid preparations, and the ease with which they clot citrated plasma is in the following order: ortho-coumarate > maleate > pyruvate > butyrate.

The next step was to test these compounds on rabbits, when I found that their power to produce dispersion, which was gauged by ultramicroscopic examinations and by measurements of the blood-sugar percentage, viscosity, surface tension and refractive index, is in a reverse order to that just given when one or two injections are administered, but in the same order when more than two are made. It also transpired that the dispersion is greater after an intramuscular than after an intravenous injection. Dispersion is accompanied by a high refractive index, by an increase in the blood-sugar and blood-urea, by an increase of albumen at the expense of globulin, by a fall in the viscosity, by a rise in the surface tension and in the suspension stability of the blood. Condensation is accompanied by the exact opposite.

The two following experiments make this point clear. An estimation of the blood-sugar percentage in a normal animal is a good guide of the degree of dispersion produced.

Experiment 1.—A rabbit received weekly intravenous injections of manganese butyrate:

Injection.	Quantity.	Blood-sugar in grm. per cent.	
First	2 c.c. 0·1 % sol.	Before injection	0·081
		Immediately after	0·081
Second.	2 c.c. 0·1 % sol.	Before injection	0·081
		Immediately after	*Blood clotted.*
Third	1 c.c. 1 % sol.	Before injection	0·115
		Immediately after	0·112
Fourth	2 c.c. 1 % sol.	Before injection	0·118
Fifth	2 c.c. 1 % sol.	Before injection	0·112
		Immediately after	0·106
Sixth	2 c.c. 1 % sol.	Before injection	0·100
Seventh	2 c.c. 1 % sol.	Before injection	0·093

Experiment 2.—A rabbit received weekly injections of manganese ortho coumarate:

Injection.	Quantity.	Blood-sugar in grm. per cent.	
First	2 c.c. 0·1 % sol.	Blood before injection	0·081
		Immediately after	0·100
Second.	2 c.c. 0·1 % sol.	Blood before	0·068
Third	1 c.c. 1 % sol.	Blood before	0·086
		Immediately after	0·093
Fourth.	2 c.c. 1 % sol.	Blood before	0·137
Fifth	2 c.c. 1 % sol.	Blood before	0·112
		Immediately after	0·100
Sixth	2 c.c. 1 % sol.	Blood before	0·125
Seventh	2 c.c. 1 % sol.	Blood before	0·100

These two experiments show that the immediate effect of manganese ortho-coumarate is dispersion, that this is followed in a few days by condensation, and that the maximum degree of dispersion is not reached till one week after the third injection. Manganese butyrate, on the other hand, produces no immediate effect, but a dispersion after the second injection which is so great as to fail to prevent coagulation upon the addition of oxalate. It may be noted further that the duration of great dispersion is short, and that as the injections are increased condensation results. The paradox between the coagulating effect *in vitro* and the action *in vivo* is thus explained.

In infections caused by simple micro-organisms where the incubation period is short and the amount of condensation to which the protective substance is submitted is comparatively trifling, I thought better effects would be produced by manganese butyrate, which has

an immediate conductor action, than by manganese ortho-coumarate, which exhibits an initial condenser effect. This proved to be the case, and several months' trial with a 1 per cent. solution injected intramuscularly in doses of 1·0 and 1·5 c.c. has shown me that manganese butyrate is the best preparation to date for use in the acute stage of coccogenic infections. In boils, carbuncles, erysipelas, including that which follows vaccination, whitlows, lymphangitis, lymphadenitis, acute gonococcal urethritis, abscess-formation and epididymitis, two injections of manganese butyrate with an interval of four clear days prove of greater value than any other method of treatment. In acute dermatitis, excluding the seborrhœic form, where contramine is indicated, manganese butyrate is useful. In asthma relief is frequently obtained in twelve hours. In my opinion asthma is due to the protein particles undergoing condensation in the pulmonary capillaries, and its relief is due to the conversion of the same into dispersion. In gonococcal arthritis contramine should be used from the start, but in cases of acute urethritis, periurethral abscess, prostatic abscess and epididymitis, the injection of contramine prescribed with the idea to reduce the fibrous tissue formation to the minimum should not be prescribed for five days after the second injection of manganese butyrate. Patients suffering from their first attack of urethritis are usually freed of their symptoms by two injections of manganese butyrate, even when no local treatment is prescribed. Experience has taught me that patients do very much better with mild syringing than with irrigations. In all septic conditions manganese butyrate should be given a chance before an incision is made. If prescribed in time the lesion will, most probably, abort; but if pus has already formed a single injection will bring it to a head. The pus should be evacuated through a small incision and dry dressings and not hot fomentations should be applied. I have had excellent results from manganese butyrate in septic hands in medical men. In carbuncles the obvious lesion may mend while the patient goes downhill, due to metastatic foci in the lungs or kidneys. That a carbuncle is often an outward sign of an internal purulent focus is not sufficiently realised. In anæmia, manganese butyrate is of some value as an alternative to iron. But owing to the chronicity of these cases, it is best to inject the drug in weekly 0·5 c.c. doses. In animals, manganese butyrate prevents intoxication with non-metallic sub-

stances and restores them to health if it is already in being. It is also both a preventive and curative agent in condenser shock, or anaphylaxis, as it is usually called. But it acts beneficially provided it is prescribed in time; if too late it will add to the intoxication and hasten the fatal issue. This is also very true of the use of contramine in metallic intoxication and in conductor shock, which is the same as intravascular clotting. If a rabbit is injected intravenously with 0·002 grm. of ergamine and again three weeks later, it dies instantaneously of shock. But if an injection of manganese butyrate is administered a week before the would-be fatal dose, the animal does not die. Manganese ortho-coumarate has an initial condenser effect, due to the fact that its molecule is bigger and more complex than that of manganese butyrate. The more complex a molecule becomes the greater is its condenser action. The groups which increase the condenser action of a compound most are the imino and amino groups. This explains why salvarsan when it is first administered causes an aggravation of the symptoms. This so-called Herxheimer-Jarisch reaction is not due to the death of the micro-organisms but to their extra activity, which is occasioned by the temporary increased condensation the protective substance undergoes. Provided the molecule contains a metallic group the conductor effect to be produced, though late, stands in a direct ratio to the complexity of the molecule. The conductor action will naturally be influenced by the metal employed. As manganese is a better conductor than arsenic, I wondered whether this advantage would compensate for the disadvantage of the more simple radicle of the ortho-coumarate compared with the amino-benzene radicle of salvarsan. I treated some cases of syphilis with a concentrated aqueous solution of manganese ortho-coumarate, with the result that the Herxheimer reaction was much more pronounced and the lesions disappeared much more slowly than is the case with salvarsan. With the hope that manganese ortho-coumarate might prove of some value in a chronic infection such as is caused by the tubercle bacillus, I have asked Dr. Adamson to be so kind as to treat some cases of *Lupus vulgaris*, and shall await his verdict with interest. There is one other condition—toxæmia of pregnancy—in which the protein particles undergo sufficient condensation to cause what may be alarming symptoms, which is relieved by the employment of conductors. But I have not had enough cases to say whether

manganese butyrate is more efficacious than manganese ortho-coumarate, or the reverse. From my work on the coagulation of the blood I have gained the idea that hæmophilia is due probably to the fact that the protein particles are not able to undergo dispersion upon withdrawal, therefore it would be very interesting to see if manganese butyrate is of any value in this condition. Perhaps those who come across such cases would give the drug a trial.

Illustrative Cases.

Case 1.—A medical man had a whitlow on the right thumb, with severe lymphangitis above the elbow and some swelling of the lymphatic glands in the right axilla. The day following the first injection of manganese butyrate the pain and swelling vanished, the sense of well-being returned, and after the second injection administered five days later the trouble completely disappeared.

Case 2.—A case of tabes developed a septic foot *viâ* a perforating ulcer. Under two injections of manganese butyrate of 1·0 and 1·5 c.c. respectively the foot returned to its pre-septic condition.

Case 3.—A patient had a double quinsy, and had had nothing to eat or drink for five days. At midday on the sixth day 1·0 c.c. of manganese butyrate was injected intramuscularly. The following morning the patient woke up feeling enormously improved and able to have a good breakfast.

Case 4.—A patient had had vaccination erysipelas for four days with a temperature of over 104° F. The day following an injection of 1·0 c.c. of manganese butyrate, the swelling and redness of the extremity had vanished and the temperature was normal.

Case 5.—A patient accustomed to have two or three asthmatic attacks a year, or whenever she caught cold, and to have great difficulty in breathing, which invariably lasted for at least five days, was able to breathe easily the day following the first injection. After the second injection the rhinitis also vanished.

Case 6.—A woman with bilateral multi-lobular mastitis completely recovered after two injections of manganese butyrate. Even when a case has been operated upon manganese butyrate will expedite healing, and should be used in such conditions as suppurative periostitis, osteo-myelitis, etc.

In boils, carbuncles and acute septic dermatitis the results are equally

remarkable. In general sepsis the drug can be employed with advantage so long as the patient is capable of resisting the infection. If the infection is getting the better of the patient the drug will do more harm than good. In plain gonococcal urethritis the pain on passing water and the chordee disappear the next day, and a week after the second injection the discharge has quite ceased. This applies equally to both men and women. Two injections do not cure these cases, so I extend the syringing and give a few injections of vaccine to be on the safe side. To date I have had over thirty cases in which the disease was caught early enough to prevent extension into the posterior part of the urethra. In gonococcal epididymitis the pain begins to get less twelve hours after the first injection.

ONE FORM OF "ELEPHANTIASIS NOSTRAS" OF THE VULVA—DIFFUSE CONNECTIVE-TISSUE HYPERPLASIA AT PUBERTY, PROBABLY ON A SCROFULO-TUBERCULOUS BASIS.

F. PARKES WEBER, M.A., M.D., F.R.C.P.

The patient, J. D—, aged 23 years, a rather fragile-looking, pale girl of medium size, with typical physical signs of slight mitral stenosis and with a condition of "elephantiasis nostras" of the vulva, was admitted to hospital under my care on June 25th, 1921. She was of a Russian-Hebrew family, but she herself had been born in London and had never been out of England. Besides the mitral stenosis there was a chlorotic type of anæmia, and a blood-count, taken later on in 1921, gave 4,220,000 red cells and 8900 white cells to the c.mm. of blood; hæmoglobin, 39 per cent. There was no fever. The Wassermann reaction for syphilis was negative. There was no history of previous rheumatism. The elephantiasis involved chiefly the labia majora, but the labia minora were likewise enlarged. The left labium majus was enormously enlarged—much more than the right one—and the left labium minus was likewise larger than its fellow The skin over both labia majora was coarse and abnormally wrinkled.

Later on, in October, 1921, my surgical colleague, Dr. M. Schroeter, excised both labia majora and the left labium minus. I have to

thank him for his kindness in allowing me to publish this note. By naked-eye examination the removed parts appeared to consist of hyperplastic connective tissue or diffuse fibromatous growth. They were given to the Museum of the Royal College of Surgeons.

The patient was readmitted on January 29th, 1923, with massive recurrence of the elephantiasis vulvæ on the left side and slighter recurrence on the right side. Dr. Schroeter excised a portion of the left labium majus as big as an orange and a smaller piece of the right labium majus. Macroscopically these pieces seemed, as before, to consist of connective tissue covered by coarse, wrinkled skin. A piece of tissue from the left labium majus, microscopically examined, was reported on by Dr. C. Fletcher as follows: "Sections have been cut of this tissue, which is composed entirely of œdematous connective tissue containing numerous fairly thin-walled vessels. There is also a certain amount of perivascular small-celled infiltration. I see no evidence of lymphangiectasis."

The patient is still anæmic. The Pirquet cuti-reaction (February 6th, 1923) gives a positive result with 50 per cent. Koch's old tuberculin. She has definite physical signs of (quiescent?) tuberculosis of the hilus and upper lobe of the right lung. The operation wounds are healed (February 12th, 1923), and she will soon leave the hospital. Open-air and general hygienic treatment against tuberculosis is to be obtained if possible. There is slight hard enlargement of lymphatic glands in the right groin. Later on local Röntgen-ray treatment will probably be tried against recurrence of the elephantiasis. In conclusion I should mention that the patient also suffers from chronic nasal obstruction, due to enlargement of both inferior turbinateds, and that she has twice had tonsils and adenoids removed, firstly at 7 years of age, and again when she was 13 years old. A younger brother of the patient was formerly treated for tuberculous disease of the knee-joint.

Remarks.

Some forms of chronic enlargement of the labia majora of the vulva may from the ætiological point of view be compared to chronic enlargement of the lips of the mouth. Therefore, in connection with the present case, when reviewing the various possible causes of elephantiasis vulvæ and chronic enlargement of the labia majora, I

shall refer to some of the known causes of macrocheilia; I shall also refer to some of the known causes of macroglossia.

(1) *Filarial, tropical, or endemic elephantiasis.*—This may, of course, be excluded in a young native of London, who has never travelled away from England.

(2) Enlargement of the labia majora or regular "elephantiasis" vulvæ, when non-filarial, is generally due to *chronic lymphatic obstruction of tuberculous, syphilitic, gonococcal or septic (streptococcal) origin.* In the present case the Wassermann reaction is negative, and various features point to the elephantiasis vulvæ being on a scrofulo-tuberculous basis, though there is absence of any lupus or superficial tuberculous lesion, and there are no definitely tuberculous lymphatic glands to be made out in the neighbourhood. I need only refer to the masterly account of "Tuberculous Elephantiasis in regard to a Case of Tuberculous Elephantiasis of the Vulva," by E. Forgue and G. Massabuau (of Montpellier), in the *Revue de Chirurgie*, Paris 1909, xxxix, pp. 1029–1052. The local lesion of the vulva consists, according to these authors, in hyperplasia of œdematous, dense connective tissue, with hyperkeratosis and overgrowth of the cutis. In regard to determining the tuberculous nature of the condition inoculation of guinea-pigs may furnish valuable confirmation. After surgical removal of the parts recurrence follows more or less rapidly in the scar or in the adjoining parts. Finally, visceral or pulmonary tuberculosis may terminate the case. In regard to the question of tuberculous elephantiasis vulvæ I would likewise refer to C. E. Purslow, *British Medical Journal*, 1911, ii, p. 999; C. Daniel, *Monatsschrift für Geburtshilfe und Gynäkologie*, Berlin, 1913, xxxvii, p. 65; D. M. Greig, *Edinburgh Medical Journal*, new series, 1916, xvii, p. 111; and A. Ravogli, *Journ. Cut. Dis.*, 1919, xxxvii, p. 38.

(3) I do not know that cases of elephantiasis of the vulva have been observed as apparently a direct result of *excision of enlarged inguinal lymphatic glands*, analogous to some cases in males of elephantiasis of the penis and scrotum.

(4) *Lymphangiomatous* and *hæmangiomatous conditions* may be excluded in the present case. They are better recognised as occasional causes of macrocheilia and macroglossia.

(5) *Neurofibromatous enlargement* can likewise be excluded in the present case. As a cause of macrocheilia or macroglossia neuro-

fibromatosis is likely to be unilateral. Compare the cases of neurofibromatosis of the tongue described by Abbott and Shattock, *Trans. Path. Soc. Lond.*, 1903, liv, p. 231; Spencer and Shattock, *Proc. Roy. Soc. Med., Pathological Section*, London, 1908, i, p. 8; F. Parkes Weber, *British Journal of Children's Diseases*, 1910, vii, p. 13. For neurofibromatosis as a cause of right-sided unilateral macrocheilia of the upper lip see the case of a girl, aged 13 years, described by J. D. Rolleston and N. S. Macnaughtan, *Proc. Roy. Soc. Med., Clinical Section*, 1911, iv, p. 71 (Case 2) and p. 114 (histological report).

(6) A variety of macrocheilia has been ascribed to *hypertrophy and hyperplasia of the mucous glands* by G. Masera (*Il Morgagni*, Milan, 1911, liii, Archivio, p. 151), but I have not heard of any analogous cause of enlargement of the vulva. Compare also J. W. Wright, "A Case of Hypertrophy of the Mucous Glands of the Lips," *New York Med. Journ.*, 1884, xl, p. 152.

(7) Many cases of macroglossia are supposed to be of purely *muscular* nature (compare P. Lengemann, *Beiträge zur klin. Chirurgie*, Tübingen, 1903, xxxix, p. 519, and R. Welzel, *ibid.*, 1910, lxvii, p. 570), but there is no recognised analogous condition in the lips or vulva. Compare, however, the cases (sometimes familial) of "macrocheilia panparenchymatosa congenita," as described by P. Cattani, *Schweiz. med. Wochenschrift*, 1923, liii, p. 85.

(8) *Lipoma* is an exceedingly rare cause of macroglossia (see V. Warren Low, *Trans. Med. Soc. Lond.*, 1912, xxv, p. 356, with coloured plate), but I do not know of it as a cause of enlargement of the lips or vulva.

(9) *Primary diffuse connective-tissue overgrowth* is a possible cause of macrocheilia, and a kind of diffuse connective-tissue hyperplasia may be suggested as a cause of elephantiasis vulvæ, analogous to fibro-adenomatous "pseudo-hypertrophy of the breast" at puberty. This, I would suggest, *in association with a scrofulo-tuberculous condition*, is the cause of the vulvar elephantiasis in the present case, though no certain proof of the local presence of tubercle bacilli in the affected parts or in the neighbouring lymphatic vessels and glands has yet been obtained. There may, however, possibly also be a chronic streptococcal factor in the case, as there is in most cases of macrocheilia. This constitutes an additional point in favour of trying Rœntgen-ray treatment.

CURRENT LITERATURE.

ANIMAL AND VEGETABLE PARASITES.

THE GLAND ACTION OF PEDICULUS PUBIS IN RELATION TO THE ORIGIN OF MACULÆ CÆRULEÆ. F. Grusz. (*Derm. Wochenschr.*, November 11th, 1922, lxxv, No. 45.)

According to this author previous results with pubic lice extracts must be regarded as fallacious, inasmuch as the whole bodies of the parasites were used in the investigations. For the purpose of his own series the heads were separated *in vivo* from the thorax and abdomen in 100 adult pediculi, and ground up in separate mortars with quartz sand, which was subsequently extracted with normal saline, human blood-serum or 3 per cent. sodium fluoride solution, so that every ·5 c.c. of the filtrate contained extracts from 100 lice. A very comprehensive bibliography, which includes such parasitological authorities as Nuttall and Strickland, Sabbatani, Falot, Oppenheim, Pellier, Delbanquo, Ciuffo and others is cited, and their results duly criticised.

Grusz, the present author, finds that the maxillary secretion acts on washed human blood-corpuscles, inhibits coagulation, and is a weak hæmolytic. He suggests the name "phthirolysin." The extract from the thoracic and abdominal viscera, *i. e.* from the mesenteric glands, which he would call "phthiriasin," on the other hand, is anti-hæmolytic and coagulative, and he finds that this substance is much stronger and neutralises the action of phthirolysin when mixed with it.

It is therefore, in his opinion, only in certain areas of the body that the *pediculus pubis* can produce the phenomenon known as maculæ cæruleæ, and these are the non-hairy regions where the skin is thin and the maxillary glands are particularly in request because the parasite must use its mouth to maintain a hold. The alteration of blood colour could not be produced *in vitro*, and in the author's opinion the macules are the result, not of a special pigment manufactured by the parasite, but are due to the local hæmolysis and the conversion of hæmoglobin into hæmatoidin. That it is not a true pigment is supported by the fact that such macules can be absorbed in from 10–14 days. H. S.

CUTANEOUS THRUSH. Kajka. (*Derm. Wochenschr.*, June 17th, 1922, lxxiv, No. 24.)

Two types are described and both occur in nurslings:

(1) A dry, tinea circinata-like type, with exfoliation and "collarette" formation (Beck).

(2) A moist vesicular eruption, in the walls and contents of which the causal agent—*Oidium albicans*, a fungus which is a sort of transitional variety between a hypho- and blasto-mycelium—can usually be found. In the vesicles with clear contents it can usually be isolated as a double-contour branching mycelium; in pustules it is broken up, and often occurs as an intra-cellular spore or gonidium (Ibrahim).

The two types are usually mixed, and vesicles are sometimes observed together with patches or "collaretted" lesions. The infection probably occurs after maceration, by a loose stool, of the epithelium on the buttocks or groins, and in such a case is usually of the vesicular type. But it can occur on healthy skin, and in such a case is clinically the dry variety—the erythema mycoticum of Beck. H. S.

DIAGNOSIS OF YEAST INFECTIONS OF THE SKIN. Alexander. (*Derm. Wochenschr.*, November 18th, 1922, Nr. 46, lxxv.)

The remarks under the above heading are based on the reports of four cases recently under the author's care.

The first—a woman, aged 60 years, with marked glycosuria—developed severe pruritus *ad genitalia*, and on examination was found to have a slightly infiltrated, partly scaly, partly moist eruption in these regions. Demarcation from the healthy skin was noted as incomplete. Additionally there was a scattered pustular eruption over the whole body, involving the follicles mainly. The mycelium of *oidium albicans* was present both in the scales of the drier parts of the genital eruption and in the roofs of the pustulo-vesicles above noted, and cultures on Sabouraud's standard medium yielded a yellowish, smooth, shiny growth of the well-known yeast colonies. With improvement in the general condition and the local application of boracic and lead compresses the eruption cleared up.

In the second case, a woman, aged 70 years, without diabetes, there was a very irritable circular plaque (five-shilling-piece size) on dorsum of right foot. The edges of the patch were raised, and a few vesicles again produced the microscopic and cultural evidences of yeast fungus. The clinical resemblances here to tinea were very close.

Case 3, female, aged 40 years, had an irritable eruption of symmetrical character on the internal aspect of both upper thighs. The elements of this eruption were ringed and scaly, and crusted to some extent. Oidiomycosis was again established in culture and by the microscope.

The eruption in the fourth case—also a woman, aged 75 years—was chiefly noted in the pubic and genital regions, and was partly dry and scaly and partly moist, as in the first case. Owing to previous treatment the characteristic sharp margin was largely obliterated, but was more pronounced on the dependent mammary skin, and laterally over the ribs. After considerable search the typical mycelial elements with their mulberry spore-bearing extensions were demonstrated and the fungus isolated in culture.

The author lays particular stress on the characteristic mulberry grouping of the spores as opposed to the chain-like extensions of segmented spore-like mycelium in preparations of the ringworm family. On the clinical side his suspicions are aroused when the eruption consists of grouped, maybe circular or crescentic, pustular or vesicular plaques, resembling tinea on the one hand and intertrigo on the other. He recommends the removal of numerous minute fragments of raised epithelium, either the scales or the roofs of vesicles or pustules, for cultural purposes, although he agrees that for diagnostic purposes the mycelium must be demonstrated in the roof of a vesicle, as well as subsequently in culture (6–8 days). H. S.

CONTRIBUTION TO THE STUDY OF TRICHOPHYTON PURPUREUM, BANG, TRICHOPHYTON INTERDIGITALE, PRIESTLEY, AND TRICHOPHYTON "B," HODGES. Masao Ota. (*Arch. of Derm. and Syph.*, 1922, v, p. 693.)

In this paper the author describes the cultivations he obtained in a series of cases of mycotic dysidrosis, dysidrotic eczema and interdigital trichophytosis. Out of a total of forty-eight successful cultivations he obtained the *Trichophyton*

asteroides once, *Trichophyton interdigitale* eighteen times, *Trichophyton gypseum* six times and varieties of the *Trichophyton purpureum* nine times, *Epidermophyton inguinale* twice, and trichophytons which could not be classified on account of the development of pleomorphism twelve times.

After an examination of the literature, together with his own investigations, Ota arrived at the following conclusions :

(1) *Trichophyton purpureum*, Bang, *Epidermophyton rubrum*, Castellani *Trichophyton* "A," Hodges, and probably also *Trichophyton rubidum*, Priestley, are one and the same organism; and as it has the character of an ectothrix it would be more apt to call it *Trichophyton* than *Epidermophyton*.

(2) The trichophyton species which Hodges has temporarily named *Trichophyton gypseum*, variety C, is most likely the same as *Trichophyton interdigitale* Priestley, and a trichophyton which Ota temporarily named *Trichophyton gypseum*, variety 2. Since no one named the species prior to Priestley, it is only right to call it *Trichophyton interdigitale*, Priestley.

(3) There are varieties of *Trichophyton interdigitale*. The first is that of Kaufmann Wolff and Curt von Graffenried. Ota also had three cases of this species and named it temporarily *Trichophyton gypseum*, variety 3. The second variety is that which he temporarily named *Trichophyton gypseum*, variety 4. This resembles *Trichophyton lacticolor* in many respects. However, the animal inoculation gave a negative result.

(4) The unidentified trichophytons which he obtained from ringworm of the glabrous skin, regarded as large-spored ectothrix, he divided into two groups: (*a*) *Trichophyton α*, which never exhibits a purple colour on the back of the cultures, and (*b*) *Trichophyton β*, which exhibits this colour.

(5) Trichophyton "B" Hodges, in part resembles *Trichophyton gypseum*, variety 4, but it seems more closely related to Trichophyton *β* in the more important qualities. J. M. H. M.

EROSIO INTERDIGITALIS BLASTOMYCETICA. James Herbert Mitchell. (*Arch. of Derm. and Syph.*, 1922, vi. p. 675.)

A case is here reported in which a Jewish woman presented a well-defined area of shiny-red epidermis surrounded by a collarette of scales, situated on the web of the third and fourth fingers of the left hand, which became fissured in cold weather.

A microscopical examination of scrapings from it revealed double-contoured spores, which showed budding here and there, and cultures from which gave creamy-white colonies of yeast organisms. Whether or not the yeast in this case were the actual cause, or a secondary contamination, the writer was not prepared to assert. J. M. H. M.

A SKIN-ERUPTION DUE TO A MOULD. Charles Russ. (*Lancet*, 1923, i. p. 77.)

This eruption affected a small group of workers employed in sorting and packing various kinds of dried fruit. The writer considers that the constant rubbing of the forearms against the sacking placed on the work benches caused the infection. This sacking had contained the dried fruit, which comes from all parts of the Orient and Colonies. On the fourth day following inoculation appears a raised red papule. This becomes vesicular on the sixth day and pustular on the eighth. The lesions were invariably situated on the palmar

surfaces of the forearms only. Smear preparations taken by the author revealed nothing very characteristic, but after 14 days' culture a fine filamentous growth developed. On examination this showed a freely branching mycelium bearing endospores. Prof. G. Massee, to whom a pure culture was submitted, reported it to be a typical "cereosporella," but one which does not correspond to any previously described variety. He suggested the name "*Cereosporella vexans*." It resembles the asteroid trichophytons.

The writer gives an illustration of the lesion caused by inoculating the fungus into his own arm, also one of a 5 weeks' growth on Sabouraud's medium.

R. P. W.

THE VARIETIES OF SCALP RINGWORM OBSERVED IN BORDEAUX FROM 1919 TO 1922. G. Petges and P. Joulia. (*Ann. Derm. et Syph.*, 1923, VIe série, iv, No. 1, p. 9.)

The authors present in tabular form the varieties of ringworm of the scalp found by them in children from 2–15 years of age during the period March, 1919, to June, 1922. The diagnosis was confirmed microscopically and culturally. Their statistics are based only on cases treated by them in hospital or private practice, and do not include a far larger number seen by them merely for diagnosis, among which were 400 children infected with the microsporon from an orphanage.

Among 176 patients the following varieties were found:

Microsporon Audouini . .	112 = 63 per cent.
Trichophyton violaceum . .	32 = 18 „
T. crateriforme	1 = less than 1 per cent.
T. gypseum asteroides . .	1 = „ „
Favus	80 = 17 per cent.

H. W. B

TINEA EXANTHEMATA DUE TO MICROSPORON INFECTION. L. Arzt. (*Derm. Wochenschr.*, December 9th, 1922, Nr. 49, lxxv.)

On a material of twelve cases of this rare complication or association of tinea tonsurans of the microsporon type, Arzt has described a typical generalised lichenoid eruption (lichen microsporicus, by analogy with Bloch's lichen trichophyticus). The *generalised* eruption was limited to children in his series, although *localised* accidental contaminations on the glabrous skin of adults were not excessively rare at the clinic which treated the children, and among their relatives. The scalp condition was not clinically identical in these twelve cases. Two showed simple scaliness only, without inflammatory change. Five reacted slightly with erythemato-squamous plaques, whilst in the remaining five there was marked pustulation and crusting, but no kerion formation.

The "lichen microsporicus" also did not present the same clinical features in all the cases. There was no pruritus, and in most cases the eruption was limited to trunk, or to trunk and limbs.

Besides a true follicular lichenoid papule, he could sometimes find vesicles and even pustules replacing them. Eczematisation occurred in one case only, and then much resembled "eczema scrofulosorum," which Arzt describes as an eczema en plaque commonly confined to the lateral aspects of the trunk.

He therefore suggests two types of microsporosis for consideration—(1) a lichenoid; (2) an eczematoid.

Microscopic examinations were positive in two cases, and cultural experiments were positive in three.

Demonstrations of mycelium or gonidia in sections were all negative.

H. S.

EXPERIMENTAL STUDY OF A PATHOGENIC ACID-FAST ACTINOMYCETE (NOCARDIA). D. J. Davis and Onfre Garcia. (*Arch. of Derm. and Syph.*, 1923, vii, p. 1.)

This organism was isolated from subcutaneous abscesses localised on the extremities of a woman. The abscesses were distributed chiefly on the left foot. They were red and fluctuating and contained a thick mucoid pus. She attributed them to wounds made by the prick of rose thorns and cactus plants with which she had worked. In the pus filamentous branching organisms were present, from which cultures were readily obtained. The organism was acid-fast and pathogenic for animals and belonged to the general group of *Nocardia*. It was Gram-negative and non-acid-fast. It was pathogenic to rabbits, rats, guinea-pigs and mice, and intravenous injection of it produced typical tubercles in the organs in rabbits. In liquid media it produced peculiar conidia-like forms.

J. M. H. M.

SYPHILIS.

EXPERIMENTS ON DIFFUSION OF COMPLEMENT. J. Kabelik. (*Ceská Dermatologie*, 1922, iii, pp. 211, 233.)

To study the conditions which influence the diffusion of complement the author superimposed various strengths of complement in the test-tubes on thin agar, to which he added as indicator highly sensitised red corpuscles. His experiments led to the following results: The thickness of the haemolysed layer was greater the more concentrated and stronger was the complement; the more sensitised were the corpuscles, the smaller was the number of corpuscles used and the less concentrated was the agar. The diffusion of complement was the fastest at the beginning of the experiment; it became rapidly slower, and ceased on the third day by inactivation of complement. Analogous experiments on the diffusion of other substances tend to lead to the opinion that the colloid particles of proteins which carry the complement quality of serum are larger in colloid particles of simple serous proteins.

Spinka (St. Louis).

SCLERODERMIA (SCLÉRÈME DES ADULTES) AND SYPHILIS. (CONTRIBUTION TO THE STUDY OF ANGIO-NEUROTROPHIC "ENDOCRINIDES OF SYPHILITIC ORIGIN.") C. Audry and L. Chatelier. (*Ann. Derm. et Syph.*, 1923, VIe série, iv, No. 1, p. 1.)

The authors refer to a previous article in the *Annales* (June, 1922), in which the meaning of the term "endocrinides syphilitiques" is indicated, and in which they point out that in Raynaud's disease and in the condition described by Pick as *érythromélie* (probably the early stage of acrodermatitis chronica atrophicans) syphilitic infection would appear to be a frequent and important causal factor. In the present article they publish two cases of generalised scleroderma, in both of which the Wassermann reaction was positive. Their first patient was a girl, aged 18 years, who had had a severe attack of typhoid fever at the age of twelve,

but no other illness; menstruation began late—at the age of sixteen—and the periods were irregular and scanty. The onset of her scleroderma was sudden, and was accompanied by pyrexia, joint-pains and violent pains in the legs; the skin of practically the entire body then gradually became sclerodermatous, and for a while the thorax was so severely involved that she was constantly dyspnœic. Some improvement, however, took place. The Wassermann reaction was positive, but it was not possible to examine the cerebro-spinal fluid, as the patient refused to remain in hospital. It is probable that in this case the patient was a congenital syphilitic. The authors make no comment on the fact that the sudden onset with pyrexia and joint-pains is more in favour of the scleroderma being due to an acute or acute on chronic infection than to a rather doubtful syphilitic taint.

The second case was a woman, aged 40 years, who had married at the age of eighteen, aborted three months later, and whose husband, probably a syphilitic, died at the age of twenty-four. From 1914 to 1919 she had symptoms suggestive of cerebro-spinal syphilis, deafness, vertigo, right-sided facial paralysis and persistent headache. In 1919 the Wassermann reaction on the blood was found to be positive, and she received four injections of novarsenobenzol and mercurial treatment with benefit. In 1920 she began to have pains in the legs, with œdema and coldness of the extremities, particularly of the left foot, on the big toe of which a blood-stained blister appeared. She was admitted to hospital, and the Wassermann reaction both of the blood and cerebro-spinal fluid was positive, and there was a lymphocytosis in the latter. She received nine injections of novarsenobenzol in the course of three months. She had previously been under treatment for hæmoptysis, wasting and night-sweats. Further injections of novarsenobenzol were given and the patient remained well for six months. In January, 1922, however, after violent headaches and swelling and pains in the legs, the scleroderma began in the arms and gradually spread. The Wassermann reaction was still positive, and an elaborate urinary analysis revealed evidence of hepatic insufficiency. Five more injections were given and thyroid was administered. The general condition improved, and the sclerodermatous tissue became softened to some extent.

From this case the authors deduce (1) that the scleroderma was probably not due to syphilitic involvement of the nervous system, as it began at a time when the nervous symptoms were in abeyance, and (2) that the evidence of hepatic insufficiency, as obtained from urinary analysis, suggests an "endocrinide hépatique" of syphilitic origin. The precise meaning of this is not clear, and they take no account of the possibility of the hepatic insufficiency being due to the arsenical injections, notwithstanding that in a footnote a brief comment is made on a case of Raynaud's disease with gangrene of the right foot in a man cured twelve years previously of a syphilitic hemiplegia, the authors remarking that "it is curious that in this case, too, the gangrene seems to have been aggravated by the administration of arsenobenzol." Since Ayres, who found arsenic in appreciable quantity in the urine of three consecutive cases of diffuse scleroderma, has suggested that the condition may sometimes be caused by chronic arsenical poisoning, the second case described in the article under review is not without significance in this connection, since the patient had already had eighteen injections of novarsenobenzol *before* the onset of the scleroderma. H. W. B.

QUARTERLY SURVEY OF DERMATOLOGICAL LITERATURE.

ERYTHEMAS, INFLAMMATIONS, ETC.

Acne Vulgaris, Rœntgen Ray Treatment of. R. JACOBY. (*Boston Med. and Surg. Journ.*, November 30th, 1922, clxxxvii, No. 22, p. 793.)

Alopecia, its Treatment. L. K. MCCAFFERTY. (*New York Med. Journ.*, October 4th, 1922, cxvi, No. 7, p. 319.)

Anthrax, 123 Cases in Pennsylvania Leather Industry. H. F. SMYTH. (*Journ. Indus. Hyg.*, June, 1922, vol. iv, No. 2, p. 53.)

Argyria, Two Cases of. G. MARANON. (*Ann. de Derm. et de Syph.*, January, 1923, No. 1, p. 35.)

Cutting Oils causing Skin Lesions, Bacteriological Study of. R. C. ROSENBERGER. (*New York Med. Journ.*, October 4th, 1922, cxvi, No. 7, p. 377.)

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Drug Eruptions, Clinical Aspect of Recent Medicaments. F. WISE and H. J. PARKHURST. (*Arch. of Derm. and Syph.*, November, 1922, vi, No. 5, p. 542.)

Eruptive Fever with Stomatitis and Conjunctivitis, illustrated. A. M. STEVENS and F. C. JOHNSON. (*Amer. Journ. Dis. Child.*, December, 1922, xxiv, No. 6, p. 526.)

Erythema Induratum treated by Ultra-violet Light. E. L. OLIVER. (*Arch. of Derm. and Syph.*, November, 1922, vi, No. 5, p. 619.)

Erythema Multiforme Bullosum, caused by Arsenic. W. J. MACDONALD. (*Boston Med. and Surg. Journ.*, December 7th, 1922, clxxxvii, No. 23, p. 847.)

Erythema Serpens (L'érysipéloide). W. DUBREUILH and P. JOULIA. (*Ann. de Derm. et de Syph.*, December, 1922, No. 12, p. 609.)

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Hydroa Vacciniforme. F. E. SENEAR and H. W. FINK. (*Arch. of Derm. and Syph.*, February, 1923, vii, No. 2, p. 145.)

Incidence of Special Skin Diseases, Statistics. S. POLLITZER. (*Arch. of Derm. and Syph.*, January, 1923, vii, No. 1, p. 99.)

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Industrial Dermatitis, Classification of. C. G. LANE. (*Arch. of Derm. and Syph.*, January, 1923, vii, No. 1, p. 77.)

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Iodide and Bromide Exanthems, Experimental Study. U. J. WILE, C. S. WRIGHT and N. R. SMITH. (*Arch. of Derm. and Syph.*, November, 1922, vi, No. 5, p. 529.)

Lacquer Dermatitis. W. A. PUSEY. (*Arch. of Derm. and Syph.*, January, 1923, vii, No. 1, p. 91.)

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SYPHILIS.

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Trépol Treatment of Syphilis. Lehner and Radnal. (*Derm. Wochenschr.*, October, 1922, lxxv, No. 42.)

Tumour, After Injection of Mercury in Vegetable Oil, Case of. I. C. Sutton. (*Arch. of Derm. and Syph.*, February, 1923, vii, No. 2, p. 223.)

REVIEWS.

X-Rays and Radium in the Treatment of Diseases of the Skin.*

This is the most complete book so far published dealing with this very important subject, and it is of particular value because it is written by a dermatologist who is thoroughly cognisant of the conditions which he is treating. Further, not being tied down to one particular group of therapeutic agents, the author is in a position to determine without bias the conditions which are likely to benefit by the use of X-rays and radium. Dr. MacKee is not open to the criticism usually levelled at dermatologists—that they are ignorant or only very imperfectly versed in the physical properties of these powerful agents. The first eighteen chapters—nearly half the book—are devoted to the description of apparatus, the physical qualities of the rays given out and the pathological results as shown by experimental methods. These chapters are extremely complete, and enter into those minute details which are so essential for the safe application of these radiations to the skin. As regards apparatus, Dr. MacKee favours the interrupterless transformer used in association with the Coolidge tube. As regards measurement of dosage he describes two techniques: the direct, or measurement by radiometer, and indirect, or arithmetical method. In the former method he uses the pastille on the skin, and as by this method the pastille only acquires four times less colour than at half distance, it is necessary to use some such radiometer as Corbett's to determine the degree of colour change. In the indirect method he uses a series of constants, and modifies his dosage only by changes in the time and distance. He points out that this latter method is preferable, but only when an apparatus is employed which is known to give a constant supply of radiations under constant conditions. This he believes is only possible when the apparatus mentioned above is employed.

The various diseases in which X-rays and radium are applicable are fully described, and the dosage recommended is that which the author has found most suitable in his extensive experience. He deals fully with the possibilities of recurrences after treatment, and gives a judicial survey of the value of treatment in each type of case. His summary of the after-effects of X-ray treatment for hypertrichosis could be read with advantage by those who still adopt this procedure.

The chapters on radium are equally full and illuminating. The value of the book is enhanced by the final chapter on the "Medico-legal Relations of Röntgen and Radium Therapy."

The publishers have expended much care in the production of the book and the large number of illustrations are exceptionally well produced.

* *X-rays and Radium in the Treatment of Diseases of the Skin.* By G. M. MacKee, M.D., Assistant Professor of Dermatology and Syphilology, College of Physician and Surgeons, Columbia University. Pp. 602. 250 engravings and 22 charts. London: Henry Kimpton, 1922. Price 45*s.* net.

X-Ray Dosage in Treatment and Radiography.*

This is a small book which can easily be carried in the jacket pocket, and which gives details of X-ray dosage under varying conditions. It is a handy little book, and should prove useful as a time-saver to workers in this branch of medicine.

A Synopsis of Medicine.†

The demand for this book, requiring a second edition within a year, amply demonstrates its value. The book is no mere "cram" book, but, as its title implies, a *précis* of modern medical knowledge. Dr. Tidy has exhibited great skill in extracting all that is important in internal medicine, and has bestowed equal care on the clinical and pathological sides of the subject. The "Synopsis" will be of particular value to those whose main work lies outside the bounds of internal medicine, but who wish to keep in touch with modern progress.

* *X-ray Dosage in Treatment and Radiography.* By W. D. Witherbee, M.D., Radiotherapist, Presbyterian Hospital, New York, and J. Remer, M.D., Radiotherapist, New York Hospital. Pp. 87. New York: The MacMillan Co., 1922. Price 8s. net.

† *A Synopsis of Medicine.* By H. Letheby Tidy, M.A., M.D., F.R.C.P., Assistant Physician to St. Thomas's Hospital. 2nd Edition. Pp. 956. Bristol: John Wright & Sons, Ltd., 1922. Price 21s. net.

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OF

DERMATOLOGY AND SYPHILIS

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LUPUS LEISHMANIASIS: A LEISHMANIASIS OF THE SKIN RESEMBLING LUPUS VULGARIS; HITHERTO UNCLASSIFIED.

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Fig. 1 shows an Oriental sore which may be regarded as typical —a single ulcer on an exposed surface of the body, manifesting itself as a papule, whose summit necroses, leaving an indolent ulcer, with irregular thickened edges, sloughy surface and granulating base, reaching the size of a sixpenny or a shilling piece. Later, as a result of an attempt at healing, the margins become shelving; the chronicity of the ulcer is indicated by a characteristic pigmentation of the skin around, which has an indigo-blue appearance. There is no enlargement of the nearest lymphatic glands.

Typical Oriental sore is not easily mistaken. Diagnosis is confirmed by finding the Leishman-Donovan body in a scraping from the ulcer. The ulcer may become multiple by auto-inoculation, but the resulting sores are of the same character as the original.

In the Near East Oriental sore heals spontaneously in about a year, but in England it does not appear to have a tendency to heal without treatment. Other clinical varieties of dermal leishmaniasis have been described besides this typical form:

(1) Ferguson and Richards in Cairo described a *verrucose* form.

(2) Cambillet and others have described a *keloid* form.

(3) A *papillomatous* form has also been described.

These forms are nodular and non-ulcerating, but the nodules are like solid warts, and they do not resemble lupus vulgaris.

A *framboesiform* variety resembling yaws, consisting of ulcers capped with yellow crusts, is said to be common in the West Indies.

The form which I record differs from all these previously recorded varieties. The photograph, Fig. 2, illustrates it. I have lately seen two similar cases, both nursing sisters, and both from Baghdad. In both the lupus-like eruption on the face followed an Oriental sore which was thought to be "cured."

History.—The history of the case is as follows: Arriving at Baghdad in March, 1920, the nurse was bitten on the cheek by an insect in September of the same year. The cheek swelled but subsided in a few days. A small puncture marked the place for three months.

In December, 1920, when she was invalided home (for tachycardia), the bite was still a small puncture, with a little dry scale. At Bombay, whilst on her way home, Leishman-Donovan bodies were examined for with negative result.

In February, 1921, when at Netley, Leishman-Donovan bodies were found, and the diagnosis of Oriental sore made. This was five months after the insect-bite. Fomentations and methylene-blue ointment were applied.

At the end of April, 1921, Leishman-Donovan bodies were again found at Millbank, where she had been transferred. Antimony ointment and boracic ointment were applied, and the sore was given one exposure to the X-rays.

About the middle of June, 1921, Leishman-Donovan bodies ceased to be found, and she was discharged from hospital apparently cured. Treatment had extended over four months. The original sore had lasted nine months. It was now healed.

In November, 1921 (fifteen months after *apparent cure*), a "tiny raised lump," which had remained, "seemed to grow larger, and other lumps appeared one by one" around the original scar.

On June 9th, 1922, twelve months after the apparent cure of the original Oriental sore, the nurse came before a Pension Board at Cheltenham Terrace. The appearance then was as shown in Fig. 2.

There were about twenty-three small, very soft, discrete nodules of a yellowish-brown, "apple-jelly" colour, which, when pinched up between finger and thumb, were quite impalpable and devoid of induration. Diascopy showed the yellow staining usually described

as characteristic for lupus vulgaris. The covering skin was thin but normal, not ulcerated nor broken. A scar marked the site of the original Oriental sore. The nodules were arranged round the scar but not in it. They spread nose-wards rather than ear-wards. There was no pigmentation, and no enlargement of the nearest lymphatic glands. Neither pain nor irritation were com-

Fig. 1.—A typical case of dermal leishmaniasis (Oriental sore).

plained of. A series of photographs was taken to record the progress under treatment.

Treatment.—The effect of treatment is shown when Fig. 2 is compared with Fig. 3. This effect was produced in six weeks, and would seem finally to negative the diagnosis of lupus vulgaris.

Intravenous injections of antimony tartrate were commenced on June 12th, 1922, and were given three times a week; the commencing dose was ½ gr., increasing by ½ gr. each injection until 2 gr. per dose were reached, and 2 gr. were continued until 30 gr. (total) had been given.

Although the nodules as such had disappeared, and the *niveau* of the affected area was on a level with the surrounding skin, there was still a dirty brownish-yellow staining where the nodules had been, and "blue bodies" were still found in the scraping, suggesting that leishmania infection still was present. After the nurse had been home for six weeks she returned and had a further course of 16½

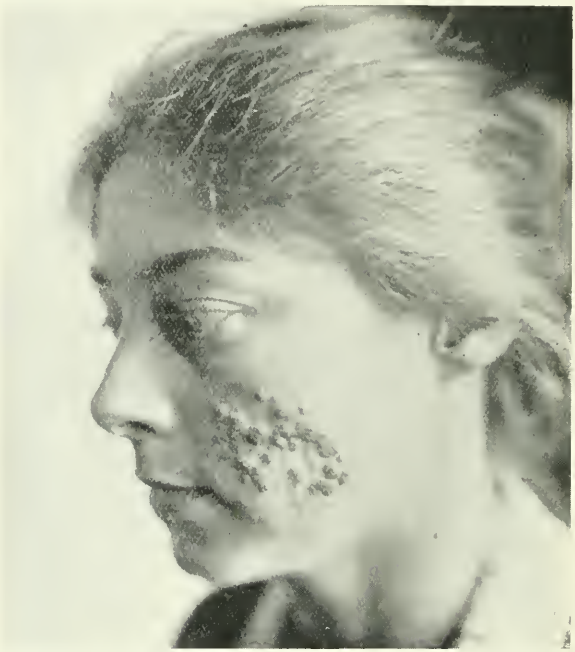

FIG. 2.—Lupus leishmaniasis. A soft yellow nodular non-ulcerating lesion. (The surface of each nodule is quite smooth—the photograph makes them appear rough.)

gr. Another interval at home was followed by another course of 17½ gr., making a total of 64 gr., and there only remained a very faint yellow stain, scarcely noticeable. The whole course of treatment, including the two intervals of eight weeks and seven weeks, lasted thirty-three weeks.*

In spite of the tachycardia she took the antimony well, and beyond an occasional headache and a little sickness and colic, and

* When the treatment commenced in June, 1922, the eruption had been present seven months and showed no signs of healing.—J. B. C.

considerable muscular pain after the injections, there were no complications, and there were no injurious results.

Pathology.—In the case under review Leishman-Donovan bodies were found only once in a scraping, after June, 1922, and they appeared to be disorganised. "Blue-bodies," which I regard as of great value in the diagnosis of leishmaniasis, were, however, con-

Fig. 3.—The same patient as Fig. 2 after a course of sod. antimony tartrate intravenous injections. The dark stains are discoloured areas which quite disappeared later. The thin white scar marks the place of the original Oriental sore.

stantly present in this lupus form of leishmaniasis. Leishman-Donovan bodies are not always demonstrable in undoubted leishmania, just as in syphilis the *Spirochæta pallida* cannot always be found. We do not know what is the fate of the Leishman-Donovan body in the body; it may be that under certain conditions it changes into "granule" form, and as such was present in the nodules (see later). The fact that the eruption followed a typical Oriental sore, and that it healed rapidly when intravenous antimony tartrate was given, is

substantial evidence for the diagnosis of leishmania and negatives the diagnosis of lupus vulgaris.

It may be said that in order to establish the diagnosis a biopsy should have been done. Apart from the fact that the lesion was on the nurse's face, and she was naturally averse to having a section made, a stained section would not have been decisive. Both lupus and dermal leishmania show giant-cell systems, and the one would not necessarily show the tubercle bacillus, and the other would probably not show the Leishman-Donovan body. The complement-fixation test for tubercle was done twice with doubtful positive result, and therefore did not help, but lupus vulgaris will not clear up in a few weeks with antimony tartrate as this eruption did.

I believe that I am recording a modified form of leishmaniasis, perhaps a residual condition, in which the virus of leishmania is not present as the Leishman-Donovan bodies, but which is a leishmania notwithstanding, and for which I would suggest the name of "lupus leishmaniasis."

The Leishman-Donovan body is seldom found in the peripheral blood in kala-azar, but thousands of Leishman-Donovan bodies are thrown into the blood-stream daily from the enlarged spleen, which is a blood-swamp in direct communication with the blood-vessels. The Leishman-Donovan bodies are broken up possibly by osmotic action (I am of opinion that some of the "blue-bodies" represent a stage in this process), the blood-stream containing leishmania virus, but in altered, it may be "granule" form. On clinical grounds it is possible that the blood, carrying a virus in another form than the Leishman-Donovan body, is infective to a biting fly, and is thus transmitted from man to man. The lupoid nodules in the same manner contain a leishmania infection which is not necessarily the Leishman-Donovan body as we are accustomed to see it. This would at least explain why Leishman-Donovan bodies were not found.

The clinical condition here described has some resemblance to cases recorded by Brahmachari as "leishmanoid." In the *Indian Med. Gazette*, April, 1922, he records four cases of kala-azar, all of which had been treated and cured by antimony tartrate (intravenous), which within six months to two years after completion of treatment developed a cutaneous eruption on face and body resembling nodular leprosy. In his cases scrapings contained Leishman-Donovan bodies. Brahmachari thought they were analogous to varioloid (smallpox modified by vaccination). The illustration of one of Brahmachari's cases does not suggest, however, lupus vulgaris. They point to the fact that a cutaneous rash sometimes occurs in cases of kala-azar after "cure," but they do not indicate that cutaneous and internal leishmaniasis are caused by the same identical organism, as he suggests.

The cases which I record point to the fact that there is a form of leishmania clinically closely resembling lupus vulgaris, which appears to occur after the original sore has been "cured" either around the site of the sore or at some distant area.

Treatment of dermal leishmaniasis.—Oriental sore is not a local disease. This is shown by one of the lupus-like cases I saw, where the original Oriental sore occurred on the right arm and the lupoidal eruption on the right cheek.

There can be no question that constitutional treatment by intravenous injections offers the most rapid and the surest method of cure for Oriental sore. Compared with intravenous antimony

tartrate, X-rays, carbon dioxide snow, antimony ointment and local remedies are of little value. Local applications which seem to do good, such as lysol, Loeffler's alkaline methylene blue, caustic potash stick, benefit because of their alkalinity. The Leishman-Donovan body abhors alkalinity, and alkaline applications are temporarily useful as a local measure. The parasiticidal properties of methylene blue are much overstated. Methylene blue penetrates the organisms of certain diseases, but does not kill the organism (bilharzia ova are stained by it, but the miracidium in the shell still lives). Moreover, it is used as an intra-vital stain (Ehrlich).

The cases of dermal leishmaniasis which appear to resist antimony tartrate intravenously—and they are few—are chronic cases where the fibrous tissue layer in the floor prevents the antimony reaching the Leishman-Donovan body in the ulcer, and these are best combated by combining the intravenous treatment with local alkaline applications as Dr. G. C. Low advises.

The danger of giving antimony tartrate intravenously has been exaggerated. I have never seen a case of fatty degeneration of the internal organs. It is surprising what large doses are tolerated by the intravenous method. It is a matter of fact that the blood-vessels and the blood constitute an organ which can withstand ill-usage as well as, or better, than any other organ. Almost any clear sterile fluid may be injected, provided it does not break up the corpuscles or irritate the lining of the veins. The blood, as is well known, is able to deal with a certain number of living organisms if, inadvertently, they should be injected.

Intravenous injection is an operation which requires care, but it is an operation which missionary society nurses are taught to do in Africa. They do it well. Selected native orderlies, who have no scientific knowledge of anatomy, or physiology, or medicine, are instructed in the method. In certain sleeping-sickness and bilharzia areas the treatment of these diseases is extensively carried out by nurses or orderlies. In view of the importance of intravenous therapy revision of the pharmacopœial doses for intravenous work is needed, for the doses tolerated by the mouth are not the same as those used in injections.

It would appear that in patients treated with intravenous antimony, when several courses are given at intervals, each course is tolerated

better than the former, but as each course proceeds the individual doses were less well tolerated, owing no doubt to a cumulative action. This is shown in minor symptoms, such as muscular pains, tendency to sickness, colic, headache, anorexia, etc.

I have to thank Dr. Henry Semon for the interest he has taken in the case and for valuable advice, and for showing it at the meeting of the Dermatological Section of the Royal Society of Medicine in June, 1922, when I was unable to do so myself.

I have also to thank Mr. N. H. Johnson for assisting me in the examinations and treatment of the case.

ARSENO-BENZOL IN THE TREATMENT OF SYPHILIS.*

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If we look back to December, 1910, when Ehrlich's *salvarsan* first was placed on the market, subsequent to the favourable reports from Alt (1), Wechselmann (2), and the numerous clinics amongst which 40,000 doses had been distributed for investigation, we shall remember that in those days the single subcutaneous or intramuscular injection of this drug was advocated in the treatment of syphilis. Clinicians, if somewhat disappointed, very soon realised that we had not in salvarsan a "therapia sterilisans magna" as was first hoped.

The intramuscular injections of "606" provoked very severe local reactions. There was produced tissue necrosis of varying degree, and a by no means negligible incidence of slough formation.† Added to this the frequency with which the dose became encysted and the variations in the rate of excretion proved that the amount and rate of absorption was very uncertain. Such was the resultant pain that patients were

* A paper read before the Congress of the Royal Institute of Public Health at Plymouth, May, 1922.

† In a series of 500 injections of "606" (I.M.) given by the author there was an incidence of 15 or 3 per cent. of abscess formation terminating in open slough (1911–1912).

known to remark that they " would sooner have syphilis than another injection."

Schreiber's (3) comparatively painless method of administering the drug intravenously as the alkaline sodium phenolic solution was readily taken up, and is employed in most clinics at the present time, subject to modifications.

Shortly after this recognition that the one injection of " 606 " was insufficient to cure came the realisation also that mercury was a very necessary adjunct. This was amply proved by Harrison and Gibbard (4) in a comparison between a series of cases treated with " 606 " alone and another series treated by the combined " 606 " and Hg. at Rochester Row.

As good examples of the treatment next to be evolved in this country might be mentioned the two following schemes which were employed by Harrison and Gibbard at Rochester Row Military Hospital (1912–1914). The first was known as the " 191 " course, *i. e.* two intravenous injections of 0·6 grm. " 606 " separated by nine weekly intramuscular injections of 1 gr. of mercury. This was supplanted by the second, which I will also describe, known as the " 15151 " course, or three intravenous injections of 0·6 grm. of " 606 " separated by two series of five weekly intramuscular injections of 1 gr. of mercury. This latter was a very popular course, and furnished good results in cases where treatment was commenced early in the infection. I have examined four cases in which the Wassermann test was found to be negative and cerebrospinal fluid non-pathological after an interval of five years had elapsed since the termination of the above course; I might add that the above tests were taken after a provocative injection of arsenobenzol, and also that in no instance was there a history or evidence of clinical relapse during the said five years. With the increase in the number of cases under salvarsan treatment came the recognition that 0·6 grm. was too large a dose to be given with safety, and most clinics favoured longer courses of smaller doses at suitably placed intervals. Following upon the original German salvarsan soon appeared the French arseno-benzol (Billon), the English kharsivan (December, 1914) and arseno-billon and the Canadian diarsenol, in this order, all of these chemically being synthetically identical, differing only in the process of manufacture. On my experience with these preparations during the past eight years, in fact over eleven years with salvarsan, during which time I have administered over one hundred thousand injections, I am unable to differentiate between them, either with regard to toxicity,

or their therapeutic value. In each of them some individual "batches" proved to be more toxic than others, both clinically and in animal experiments. Looking back at old records one would say that we met with rather more reactions following intravenous injections of the original salvarsan than in similar numbers of the other "606" preparations used subsequently. Apart from the greater potency of the earlier batches of salvarsan this also could be explained readily by the modifications in the technique which had evolved by the time these later preparations were being used extensively—modifications not only in the dosage and the intervals at which the injections were given, but also in the preparation of the solution injected. With the extreme care taken by the manufacturers, and the increased stringency in the animal controls for toxicity, there is less variation in individual batches to-day.

Ehrlich's presentation of *neosalvarsan*, "914," which he produced by treating "606" with the reducing agent, sodium formaldehyde sulfoxylate, greatly simplified the process of administration owing to the rapidity with which the preparation dissolves in water, forming a neutral solution suitable for immediate injection. Again, "914" can be introduced in a far more concentrated solution intravenously than "606," for whereas "914" is frequently given in a dilution of less than 2 c.c. per decigram, "606" is best tolerated at a dilution of 30 c.c. per decigram. The French then produced novarseno-benzol (Billon), the English novarseno-billon and neokharsivan, and the Canadians neodiarsenol.

In the latter half of 1914 Ehrlich brought out *salvarsan natrium*, "1206," which roughly is a dry form of "606" solution after alkalisation to the sodium phenolic salt. It therefore only requires to be dissolved in distilled water, or 0·4 per cent. saline, forming an alkaline solution ready for immediate use. In a limited experience with this preparation, one has found it to be very simple to administer, well tolerated, producing less reactions than the other "606" preparations after intravenous injections, and at least as efficacious.

With regard to *galyl*, which was introduced by Mouneyrat (5) in 1913, one found that its effects on spirochætes in early syphilitic lesions and in clearing up such lesions was equal to that of "606" and of "914" in equivalent doses. However, in the writer's experience it influences the Wassermann reaction to a less degree than the "606" or "914" preparations, and clinical relapses are by no means uncommon in following up cases in which it has been employed. In the form of an emulsion pre-

pared for intramuscular injections, the writer found that it failed to clear the spirochætes from surface lesions as rapidly as the "914" when so administered. One was able to detect live spirochætes in fifteen out of seventeen cases examined eighteen to twenty hours after an intramuscular injection of galyl. (The dose employed for the test was 0·3 grm. in two cases and 0·4 grm. to the remainder.) Spirochætes were again detected in two out of four of these cases eighteen to twenty hours after a second injection given one week later. Ravaut's (6) report upon the side effects of galyl in a series of upwards of 8000 injections proves that it is certainly at least as toxic as "606" and "914" preparations.

Luargol is a combination of "606" with antimony and silver introduced by Danysz. It was favourably reported upon by Renault, Fournier and Guenot (7), who stated that luargol influenced the surface spirochætes in a series of 5000 early cases to an extent equal to that of twice the dose "606," both in the disappearance of the spirochætes and the healing of the lesions.

In my own experience with the original luargol, its employment had to be discontinued on account of the local thrombosis following intravenous injections and the consequent risk of embolism. In several cases the thrombosis was sufficiently extensive to be alarming. Patients always complained of pain along the veins during an injection. The solution was strongly alkaline after the requisite amount of caustic soda had been added, and this was the probable cause of the local damage to the endothelium, although a dilution of 100 c.c. per 0·1 grm. did not prevent thrombosis. However, in this series of cases (approximately twenty) there was a complete absence of toxic effects, and the cases did well clinically in which it was possible to administer the initial course of seven weekly injections.

The introduction of *disodo-luargol* eliminated the above disadvantages of luargol. It can be injected concentrated similarly to the "914" preparations—than which it is far more stable. It is extremely well tolerated. Out of a series of approximately fifty cases there was only one incidence of punctate erythema which resolved without exfoliation. In nearly every instance one was unable to detect *Spirochæta pallida* in surface lesions eighteen to twenty hours after the first intravenous injection of 0·2 grm. in primary and secondary cases, and the influence on the Wassermann reaction was very encouraging. However, there was one outstanding case in which I was able to find spirochætes in a

papule even after the third weekly injection of 0·2 grm. Clinically, one was most impressed by the rapidity with which the later secondary syphilitic lesions responded to this drug, *e. g.* papulo-pustular, papulo-crustaceous, rupial and framboesial types, which cleared up more rapidly than in one's experience when using "914" or "606" in such cases. It is unfortunate that one is unable to procure further supplies of this drug in view of the favourable reports from the various clinics as to its convenience, stability and efficacy.

Sulfarsenol is a more recent arseno-benzol preparation very similar in composition to the "914" series, over which it possesses the great advantage of being extremely well tolerated when administered subcutaneously. Excepting in the case of a very thin or emaciated subject, where there is a deficiency of subcutaneous fat, the minimum of discomfort is produced by employing Wechselmann's [19] deep subcutaneous method of injecting the concentrated aqueous solution (0·42 grm. in 1 c.c.) just superficial to the fascia covering the gluteal nuscles, as he advocated with neo-salvarsan. When injecting the product intramuscularly, my experience has been the same as that reported by Harrison [8]—namely, a local reaction as indicated by stiffness and aching, varying in intensity from twelve to seventy-two hours after administration. Occasionally it has produced immediate severe neuralgic pain passing down the sciatic, suggesting irritation by contact with a recurrent branch of that nerve when so administered. In March, 1920. the writer tested the efficacy of sulfarsenol when introduced intravenously. Six cases of primary syphilis were selected in which the characteristics of the chancre most nearly approached a clinical uniformity, in all of which *Spirochæta pallida* was demonstrated by dark-ground illumination. To each was administered intravenously 0·42 grm. sulfarsenol dissolved in 10 c.c. aq. dest., and in five out of the six cases active spironemes were detected in the chancre serum eighteen to twenty hours later. After a second injection of the same dose given one week later live spironemes were detected in three, one of which was the case in which they were not found after the first injection. These results compare very unfavourably with those obtained from 0·3 grm. "606" or 0·45 grm. of the best "914" products when given intravenously—many batches of which I have tested in the same manner. Burn [9] and others carried out an investigation to compare the effect of sulfarsenol injections on trypanosomiasis in mice when given *intravenously*, with the effect when given *subcutaneously*. They found that, given subcutaneously, the dose

of 0·03 mgrm. per gramme weight was effective in removing trypanosomes from the peripheral blood in seventy-two hours in every instance, whereas the same dose given intravenously failed to remove the trypanosomes in any of the mice. From its chemical composition one would expect that the stability of sulfarsenol would be such that the intramuscular or deep subcutaneous method of introduction would be the more efficacious. This was amply borne out in my second, and much larger, series of cases treated by the deep subcutaneous method. Out of the first twelve primary cases, *in only one* was I able to detect spironemes in the chancre eighteen to twenty hours after the first injection of 0·42 grm. It is only fair to state that in this instance the spironemes were non-motile and apparently dead in a specimen obtained from the depth of an incision made into the densely indurated chancre. The course scheduled for primary and secondary cases consisted of seven consecutive weekly injections, commencing with three doses of 0·42 grm., followed by four of 0·6 grm. After a fortnight's rest under iodides three more weekly injections of 0·42, 0·6 and 0·6 grm. were followed by a similar three injections after another fortnight under iodides. Thus a series of thirteen injections totalling 4·5 grm. sulfarsenol was administered. One grain of mercury was given intramuscularly on the same day as the sulfarsenol. This course has given very good results to date. Of the twelve primary cases mentioned none has relapsed clinically, and the Wassermann reaction has remained negative over an average period of continuous observation exceeding one year. In ten cases of secondary syphilis, comprising six cases exhibiting profuse skin and mucous membrane lesions of from three to five months' duration, two cases of late secondary syphilis of six months' duration, and two cases of relapsing condylomata, without previous treatment, of eight and ten months' duration approximately, the results have been extraordinarily good. The lesions have cleared rapidly, and the Wassermann reaction, in every instance ++ at the commencement of treatment, has been converted to negative. The test was taken at weekly intervals from the beginning, for the first eight weeks, thereby rendering the results more reliable, and also being a very interesting indication as to progress. Only two cases of tertiary syphilis of respectively twelve and twenty-five years' duration were treated in this series. The Wassermann reaction was uninfluenced by the first seven injections. The cutaneous lesions, which in each case were of the nodular cutaneous variety, however, healed quickly. Owing to demobilisation

the sulfarsenol course, unfortunately, was not completed. In cases of syphilis of the central nervous system—especially tabetics—the writer is obtaining good results, as evidenced by examination of the cerebrospinal fluid, by supplementing deep subcutaneous injections of 0·3 grm. sulfarsenol with alternate intravenous injections of 0·3 grm. silbersalvarsan. The initial intensive course of twelve bi-weekly injections, comprising six of each preparation, is given in six weeks, during which period a diet is ordered rich in carbohydrates to ensure a constant supply to the glycogen storage in the liver and tissues, thereby fortifying the liver's resistance to withstand damage from the toxic effect of the arsenobenzols. During and after such a course very careful scrutiny is kept for early signs of intolerance. Lumbar puncture is performed once a week with the main object of increasing the extravascular penetration of the arseno-benzol derivative into the parenchyma of the central nervous system by frequent drainage, and the resultant lowering of intra-meningeal pressure. A specimen of the cerebrospinal fluid is examined on each occasion with regard to the Wassermann reaction. cell count, and globulin estimation. After a six weeks' rest under mercurial inunctions and iodides, half the above course is repeated, followed by three months' rest, when further treatment is regulated according to progress. With regard to toxic effects from sulfarsenol, the writer has experienced no incidence of exfoliative dermatitis, jaundice, or cerebral symptoms in his cases to date out of his admittedly small total of slightly over 1500 injections. Burn (9) and his collaborators were unable to detect any difference in the toxicity of sulfarsenol whether injected intravenously or subcutaneously, the maximum tolerated dose in each instance being 0·4 mgrm. per gramme mouse weight.

Silbersalvarsan.—In the hands of the writer this preparation is giving very satisfactory results to date, especially, as already mentioned, in cases of parenchymatous involvement of the central nervous system. For the past seven months the initial course of silbersalvarsan I have employed for primary and secondary cases is as follows, and have had, as yet, no occasion to modify same: On the first day 0·2 grm., the seventh day 0·25 grm., the fourteenth day 0·3 grm., with 1 gr. mercurial injection each time; the 0·3 grm. dose plus 1 gr. of Hg. is then continued every seven days up to the hundred and fifth day. Wassermann tests are made on the sixty-third and hundred and fifth days.

The vasomotor disturbances rapidly following intravenous injections,

which were frequent at first, are now rarely met with on increasing the dilution and injecting the solution more slowly. Another point I have found to be of practical importance in eliminating mild side effects is that the syringes used in the clinic require very thorough cleansing after each injection, as there is a marked tendency for the solution to form a very tenacious film on their inner surfaces, which on oxidation must increase the toxicity if allowed to remain. One has not met with any severe reactions as experienced by Dreyfus [10] with tabetics whilst they are under silbersalvarsan. I am not in favour of the technique for injecting silbersalvarsan as advocated by Karl Stern [11]. A concentrated warm aqueous solution of 2 to 3 c.c. is placed in a 10 c.c. syringe. On puncturing the vein, blood is withdrawn to complete the 10 c.c., which is then returned to the vein mixed with the drug. Emptying the contents of the syringe into a beaker of normal saline at body temperature instead of the vein, after allowing fifteen seconds to elapse, convinced me that this method is by no means devoid of risk of blockage of the pulmonary end-vessels. As compared to neosalvarsan, each ampoule of silbersalvarsan carries with it a guarantee that it has been chemically and biologically tested in the Georg Speyer House, Frankfurt.

I have, as yet, met with no developments of dermatitis, jaundice or cerebral œdema, but, as stated, this only covers a series of sixty to seventy cases under a maximum period of seven months' observation.*

Comparison between "606" and "914."

In attempting to draw up a comparison between the "606" and "914" groups of the arseno-benzol preparations as to their relative merits in the treatment of syphilis, I am firmly convinced that "606" is of greater therapeutic efficacy than the "914" products when administered in equivalent doses intravenously (Ehrlich's ratio). This is less marked in early than in later cases where the infection has progressed for three months onwards in the absence of treatment. In such cases the spirochætes have had ample opportunity to reach relatively avascular sheltered recesses unchecked other than by the varying and always inadequate production of antibodies. The slower elimination of the "606" pre-

* During the eight months since this paper was written (May, 1922) this total has increased to over 300 cases, amongst which have occurred—two instances of toxic jaundice (recovered), one severe herpes labialis, one punctate erythema (resolved without exfoliation). January, 1923.

parations, after injection, and therefore the greater likelihood of a large proportion being converted into the spirochæticidal derivative, is the probable explanation. In old-standing and commonly called intractable cases, the "606" preparations hold out a better chance of converting a positive Wassermann to a negative reaction in the blood than do the "914" preparations by the intravenous route. That, in the case of "606," excretion is slower after intravenous administration than with "914" has been adequately proved by several workers.

Stühmer [12], in his very interesting experiments, was able to demonstrate the presence of some active derivative in the blood-serum of a rabbit following an intravenous injection of "606" up till the seventh day. As compared with "914," however, he was unable to detect such derivative after the second day. He investigated the protective property of the serum against trypanosome infection of mice. He found that so long as there was any protective property remaining, the blood-serum gave the Ehrlich-Bertheim reaction chemically for "606."

Dale [13] and his collaborators, employing a modification of Voegtlin and Smith's [14] method, working with mice infected with *T. equiperdum* found that the minimum curative dose gave a uniform value of 0·01 mg. per grm. mouse weight for the different British or German preparations of "606," as compared with exactly twice the amount required when using the best proved "914" preparations. Castelli [15] found "606" to be 1·5 times more effective than "914" in rabbits inoculated with syphilis, and 1·78 times more active in spirillosis in fowls than "914." Schamberg, Kolmer and Raiziss [16], working on rats infected with trypanosomes, found "606" to be 1·74 times more efficacious than "914." Most workers agree substantially as to the greater uniformity with the "606" preparations, both as regards toxicity and therapeutic efficacy, as compared with the different "914" preparations.

From its initiation there is no evidence that the same care was taken with the German neosalvarsan to eliminate undue toxicity such as Ehrlich insisted upon with salvarsan. He pointed out that such was the variation in the toxicity of different batches of salvarsan (which could not be controlled chemically), that each individual batch made in Germany was consequently tested biologically at the Georg Speyer House, Frankfurt, prior to distribution to the profession. Each ampoule has carried with it a statement to that effect. There is no such guarantee that neosalvarsan has been similarly tested, though made in the same factory.

What is of equal importance is the fact that neither preparation appears to be subjected to a test for therapeutic efficacy. The manufacturers in the allied countries who set out to produce " 606 " during and since the war have been eminently successful, feeling their way carefully under the guidance of the specifications laid down in the patent of the German salvarsan, and submitting every batch to animal controls for toxicity. There has not been, however, the same conformity in the manufacture of the " 914 " preparations, and as Dale ([13]) points out, the patent specifications are less adequate in detail, and in fact the formula is purely theoretical, so much so that were " 914 " to contain as much arsenic as represented in the formula it could not be administered with safety in the doses advocated. With the object of safeguarding the public when so many various preparations of " 606 " and " 914 " were allowed on the market uncontrolled by any accepted standard, either with regard to toxicity or therapeutic efficacy, the Board of Trade early in 1915 requested the Medical Research Committee to carry out the biological testing of such preparations then being advertised, and used in this country. Dale and his collaborators, who undertook this investigation, found a fair amount of uniformity existed with regard to the toxicity of the different " 606 " preparations, but very considerable variations in the case of the " 914 " series.

Accordingly, after a series of experiments, it was decided that " only such batches (of ' 914 ') should be allowed to be issued for therapeutic use as were tolerated by mice on intravenous injection in a dose of 0·3 mgrm. per gramme body-weight—each batch to be tested on five mice, and if more than one mouse should die, or develop definite bad symptoms, the product to be rejected." Employing the above as a criterion, Dale found that the different " 914 " preparations under investigation could be classified under two well-defined types: (*a*) those resembling the German neosalvarsan in appearance, solubility, and rapidity of oxidation on exposure to air; (*b*) those of the other group which exhibited a more rapid and complete solubility in water, and were more stable in such condition.

On comparing the toxicity he found that many of the first group would only just pass the test—several indeed actually failed—in fact a slight raising of the standard would have excluded nearly all. Whereas with those of the second group many were tolerated in a dose of

0·5 mgrm., some even at 0·6 mgrm. per grm. mouse weight, *i. e.* they were roughly only half as toxic.

If one were to enlarge upon Dr. Dale's test with the object of rendering the same more comprehensive, I would like to suggest that a second injection of, say, half the initial dose be given to each mouse at a suitable interval with the view to differentiate by tolerance to the cumulative effect.

As might be expected, clinicians favoured those preparations of "914" giving a rapid clear solution, well tolerated in high concentration, with a low incidence of, at any rate, immediate side-effects, *i. e.* those coming under group (*b*). The demand for such stimulated the manufacturers to concentrate on the production of "914" of low toxicity. It was not long, however, before the opinion grew, as evidenced by the adverse reports reaching the Salvarsan Committee (which had now been appointed by the Medical Research Council), that these recent endeavours on behalf of the manufacturers to lessen the toxicity had also lessened the therapeutic efficacy. At this period the writer was experiencing some very disappointing clinical relapses with out-patients amongst secondary cases, occurring shortly after completion of an initial course of seven intravenous injections (3·75 grm.) of a popular "non-toxic" "914" preparation. In fact, in one instance condylomata ani developed even during the course. As the results we were obtaining at Rochester Row Military Hospital were also unsatisfactory, Major White and I readily complied with Dr. Dale's invitation to carry out investigations in syphilitic patients concurrently with a parallel series of experiments to be conducted in the medical research laboratories, in which the same preparations of "914" were to be used in mice infected with *T. equiperdum*.

As I pointed out (*Lancet*, April 22nd, 1922), "hitherto no experimental work has been carried out of sufficient importance to prove or disprove that the results obtained in treating trypanosome-infected mice with arsenobenzol form a true indication of the spirochæticidal value of such drugs in syphilitic patients. In fact, opinion has leaned towards the assumption that no reliable comparison could be drawn between the results so obtained when dealing with different organisms in such different soils." The detailed report of these investigations was published in the *Lancet* recently, and it will suffice for this paper to enumerate briefly the chief facts one felt had been proved.

(1) Certain popular preparations of "914" being manufactured and used in this country were seriously defective in therapeutic power, one preparation showing approximately only two-fifths and another two-thirds the activity of the German neosalvarsan.

(2) Preparations of "914" from the same two British sources as the above, tested after the method of manufacture had undergone modification with the object of increasing the therapeutic efficacy, showed in the one case results equal to, and in the other slightly better than the German product experimentally.

(3) In each instance where a certain preparation made a bad showing with regard to spirochæticidal activity in syphilitic lesions in man, a corresponding diminished activity was observed in trypanosome-infected mice, and *vice versâ*.

(4) On arranging the preparations of "914" which were tested by each method in their order of merit, it was found that the order was identical under each method.

To quote Dr. Dale's summing up, "No closer correspondence could be expected under the conditions of the comparison, and the correspondence obtained is so good as to justify, in our opinion, the conclusion that the determination of the therapeutic action on mice infected with trypanosomes is, at least, a very valuable index, if not an accurately quantitative measure, of the therapeutic activity of different ampoules of a preparation such as '914' on syphilis in man. The method has, accordingly, been put into routine use in the Medical Research Council's Department of Biological Standards at Hampstead, an occasional check of therapeutic activity being thus imposed, in addition to the regular testing of every batch of such products for absence of undue toxicity."

A Comparison of the Methods of Administration of the Arseno-Benzols.

Deep Subcutaneous, Intermuscular and Intramuscular Injections.

On looking back to the days when the original salvarsan was administered by the above methods of injection, I am convinced that one met with more cases in which the rapidity with which severe lesions healed was almost phenomenal than one has experienced subsequently when employing the intravenous method, and even allowing for the greater

potency of the earlier batches of the original product. The reason for these methods falling into disuse and being supplanted by the intravenous was not so much that the latter was considered to be the more efficacious, dose for dose, but mainly on account of the very considerable reduction in the amount of discomfort to the patient. As a proof of the efficacy of the old intramuscular injections of "606," I will mention five patients whom I treated privately in later 1911. Each received three injections of 0·6 grm. "606" intramuscularly at intervals of three weeks followed by two years under mercurials alternating with iodides.

Three were primary, and two of them secondary cases, and each was verified by detection of *Spirochæta pallida*.

In each instance the Wassermann was negative taken one week after the third injection of "606" and has remained negative, since I have seen each of these five patients in the present year of 1922, and taken the Wassermann after a provocative injection of "914." One of the primary cases contracted an undoubted second infection of syphilis in 1916, presenting a chancre at a fresh site, after an incubation period of approximately three weeks, in which I detected *S. pallida*. I examined him very thoroughly in order to be able to exclude a clinical relapse, and his Wassermann at the time was negative, and remained negative on the fifth day after his first intravenous injection of 0·3 grm. kharsivan, with which drug I treated him for his second infection by a prolonged intravenous course of thirteen injections totalling 5 grm.

The writer would emphasise the importance of the five cases just recorded from a point of view of prognosis in that they have been kept under observation for a period exceeding ten years.

Evidence such as the above has made one feel that it is a pity that no really satisfactory technique has been devised by means of which "606" could be injected into the tissues direct with less local damage. In early 1911 (*Guy's Hospital Gazette*, December, 1911) the writer experimented with different schemes for putting up various acid, alkaline and neutral emulsions of "606" combined with local anæsthetics, but with the best the patient usually required much moral persuasion with subsequent injections.

The excellent clinical results one saw in early cases where, say, three intramuscular injections of 0·6 grm. "606" were tolerated without gross tissue necrosis followed by final absorption, is usually explained by the slowness of excretion. With an estimated solubility of but one in

one thousand in tissue juice, one would expect that ample time and opportunity is provided for the conversion of practically the whole of the injected dose into the active derivative prior to final excretion. In my series, mentioned elsewhere, in several instances where the test was performed, arsenic could be detected in the urine up to three months after a single intramuscular injection of 0·6 grm. " 606," which is in agreement with the findings of other workers. One felt, therefore, that the spirochætes were under " continuous fire " for a longer period after an intramuscular injection than that following an intravenous. Clinically in cases where insufficient dosage of " 606 " intramuscularly was followed by a relapse, my experience has been that such relapses developed at a later date than those following an equal and usually larger dosage of the drug when administered intravenously when the excretion is more rapid. In 1916 *Colonel Harrison*, always a strong advocate of the efficacy of the old intramuscular injections of " 606," decided to give the " 914 " preparations an extensive trial by the deep subcutaneous method, since they held out promise of being much better tolerated by the tissues locally. *Riebes* [17] had reported that he was able to find only a trace of " 914 " in the tissues at the site of injection in animals after twenty hours had elapsed, as compared with similar injections of " 606," of which he could detect the presence ten weeks later. *Swift* [18] reported that less necrosis was produced by " 914 " locally in muscle than by " 606," and that absorption of " 914 " was at least six times as rapid as " 606." Accordingly Major White and the writer carried out the clinical work of an investigation at two different hospitals as to the merits of " 914 " given by the deep-subcutaneous method in comparison with " 606 " given intravenously. On combining the results which had been arrived at independently, Colonel Harrison came to the following conclusion :

(1) The intramuscular or subcutaneous injection of neo-salvarsan, novarsenobenzol or novarsenobillon is superior in immediate therapeutic effect to that of the intravenous injection of salvarsan, kharsivan, arsenobenzol, or arsenobillon.

(2) Spirochætes disappear from syphilitic lesions just as rapidly after the first intramuscular as after the first intravenous injection, and that the negative Wassermann reactions at the end of the course were 12 per cent. better after the intramuscular or deep-subcutaneous injection of " 914 " preparations than after the intravenous " 606 " preparations in

the two parallel series of similar cases treated with equivalent dosage respectively.

(3) Solution of the dose of neosalvarsan in 1 c.c. of 4 per cent. stovaine and emulsion in creo-camph cream eliminates discomfort sufficiently to make the intramuscular injection of neosalvarsan practicable for routine use.

The details of the investigation were published in the *British Medical Journal*, May 5th, 1917.

At first it was feared that the slower dissemination of the drug when thus administered would lessen the rapidity of sterilisation of surface lesions as compared with the intravenous method—a point of great sociological importance. That this is by no means the case, however, was adequately demonstrated by the following figures. Out of a total of 126 cases, in each of which the *Spirochæta pallida* was detected in a lesion prior to the first subcutaneous injection, in 123 spirochætes could not be found eighteen to twenty hours later. The initial dose in a large majority of these cases was 0·45 grm. "914." In no instance were spirochætes found forty-eight hours after the first injection. In some other cases we were unable to detect *S. pallida* eighteen to twenty hours after even 0·2 grm. "914" injected subcutaneously. The above results show a more rapid and certain sterilising effect than that obtained in the writer's experience with intravenous injections of 0·3 grm. "606." In addition to this investigation, based upon the very careful observation of 161 cases treated by "914" subcutaneously, we have treated similarly many more cases subsequently with equally good results, and the total of injections must exceed 2000 considerably. If we were able to obviate entirely the local pain, the deep subcutaneous injection is obviously the ideal method of administering arseno-benzol to the out-patient. By inserting the drug by Wechselmann's ([19]) technique superficial to the fascia covering the gluteal muscles, a myositis and resulting stiffness are avoided and absorption is very satisfactory, but by no means yet devised can we render the injection no more painful locally than the intravenous.

The incidence and the amount of such pain are always largely subject to the personal equation—what one patient will term discomfort, another will describe as torture and *vice versâ*. But it is the possible 1 per cent. or 2 per cent. incidence of torture which is so detrimental to the regularity of out-patient attendances at a clinic. However, as indicated when discussing *sulfarsenol*, progress is being made in the direction of lessened local reaction with the newer preparations.

A method which produced a minimum of discomfort in my experience, but it is impracticable with out-patients, is a reversion to the original concentrated solution of the dose of "914" in 1 c.c. of distilled water injected deep subcutaneously, the difference being that the injection is made whilst the patient is in bed, from which (to ensure complete rest) he is not allowed to move until the following day. Gentle massage is given on the second and third days to assist absorption, during which he returns to duty. There are advocates of this method in the Navy.

The rate of excretion of "914" when injected subcutaneously is very similar to that following an intravenous injection of "606." The "914" preparations, therefore, in addition to being less irritating to tissue, also have the advantage of being more rapidly excreted than the "606" preparations when the latter are injected subcutaneously, in which case the excretion is very slow and uncertain as previously stated. One feels, therefore, that there is less risk of encountering toxæmia from a cumulative effect when employing the "914" than with the "606" preparations for subcutaneous injections.

Another method of administering "914" subcutaneously was tried by the writer subsequently to Colonel Harrison having tested the same on rabbits with regard to toxicity. With the object of employing a protective medium likely to be well tolerated by the tissues, we used human blood-serum, free of cells and hæmoglobin, preferably taken from an old-standing tertiary syphilitic likely to be rich in antibodies. The dose of "914" is first dissolved in 1 c.c. of distilled water, to which is then added the serum to the proportion of 1 c.c. per decigram. After thorough mixing it is heated in a water bath for half an hour at 37° C., and then for an hour at 56° C., when, on cooling to body temperature, it is ready for deep subcutaneous injection. In addition to sterilisation, the salvarsanised serum is heated to render it more spirochæticidal, as was shown to be the case by Swift and Ellis[20].

From an initial dose of 0·1 grm. we cautiously increased, until finally 0·6 grm. "914" was administered and found to be well tolerated with absence of toxic symptoms. In a previous series of cases, in five instances an abscess developed at the site of injection from which was grown *Staphylococcus albus*. After the technique was modified to that as described above we met with no further abscess formation, though there was occasional local pain of a mild character, and absorption was satisfactory. With regard to the therapeutic tests, the first six patients

received 0·1 grm. "914," and *Spirochæta pallida* could be detected in five of them eighteen to twenty hours later. One case received 0·15 grm. and spirochætes were found after same: the next case received 0·2 grm. and one non-mobile spirochæte was discovered at the fourth examination. Twelve cases received 0·3 grm. in serum and spirochætes were not detected in any eighteen to twenty hours afterwards. The subsequent initial course comprised six weekly injections of 0·3 grm. To cases later in the series 0·45 grm. was given weekly and a few received 0·6 grm. for the last three injections. The effect on the Wassermann reaction was striking: in some later secondary cases it was converted from strong positive to negative by the week following the last injection. Each received in addition a weekly injection of 1 gr. of mercury. The writer employed the same technique extensively for *subconjunctival injections* in a series of cases of interstitial keratitis, giving finally 0·6 mgrm. "914" in 10 minims of serum at weekly intervals with good results and no local disturbance. Also a large number of *intrathecal injections* were given chiefly to cases of G.P.I. and tabes, using 0·2 mgrm. "914" in 10 c.c. serum. The results obtained in the tabetics have been very encouraging and I am still continuing with them.

I have frequently been impressed by the rapidity with which the Wassermann reaction, which has remained persistently positive in cases under prolonged intravenous courses of "914" and "606," has been converted to negative on changing from the intravenous to the intramuscular or deep subcutaneous injections of "914." Less frequently has one seen the Wassermann influenced by the reverse order in treatment. A striking instance clinically was a case (*Journal of the Royal Army Medical Corps*, April, 1915) of severe tertiary syphilis in which extensive and rapid necrosis of the bones of the hard palate, right nasal fossa, antrum and orbit was unaffected by intravenous injections of neosalvarsan and original salvarsan combined with mercurials and iodides. In fact he was getting rapidly worse. His condition commenced to improve almost at once when I gave him a course of intramuscular injections of *hectine* This was apparently a case in which the patient was unable to convert sufficient of the arseno-benzol to be therapeutic into the spirochæticida derivative when the drug was introduced intravenously. I feel confident that had I employed the same drugs ("914" or "606") intramuscularly a similar striking improvement would have occurred as with the hectine when thus administered. The above, and additional facts, have made

the writer a strong advocate, for some time past, of the combined subcutaneous and intravenous routes of administration of the arseno-benzols in the routine treatment of every case. The subsequent results from such courses have strengthened my belief in the efficacy of this scheme, an example of which is described in more detail in the treatment of central nervous syphilis under sulfarsenol and silbersalvarsan.

Concerning the *intermuscular* injections advocated by some workers, I have yet to meet the surgeon capable of performing the feat with any degree of certainty. To be able to ensure that the point of a needle is lying between two muscles and not in the substance of either when making an injection calls for no ordinary anatomist. In comparison the *deep subcutaneous* injection is an extremely simple procedure which can be performed with accuracy after a very limited experience. One very simple means of ascertaining the exact level is to plunge the needle obliquely through skin and subcutaneous fat into the muscle. If the needle be now slowly withdrawn, at the same time elevating the point towards the surface, a distinct "click" will be felt just as the point is liberated through the hole in the fascia covering the muscle. Another and equally simple plan is to pinch up a roll of skin and subcutaneous fat between the thumb and fingers of the left hand as with the "scruff" of a dog's neck. The needle is now inserted obliquely to the surface and propelled in the long axis and towards the base of the elevated skin and fat. On approaching the surface of the muscle, if the point of the needle be swept from side to side, as if dissecting the fat off the muscle, the fascia can be distinctly felt as the needle-point scratches over its superficial fibres.

(*To be continued.*)

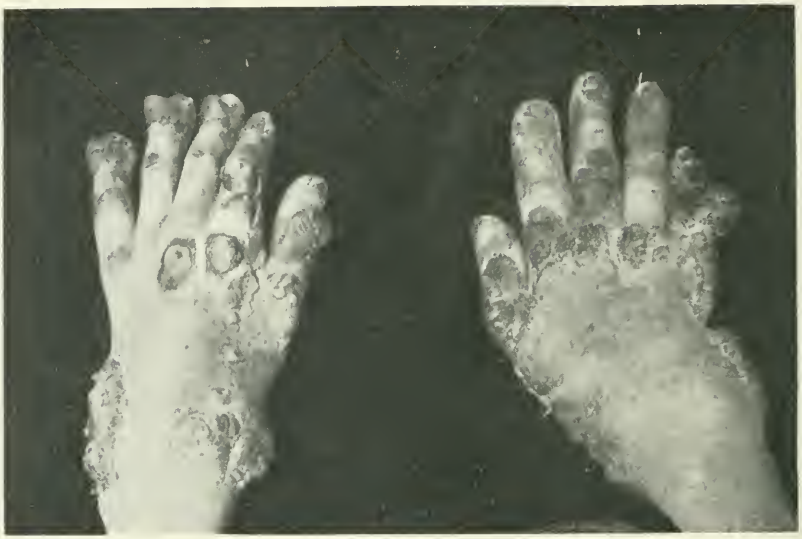

Fig. 1.

Fig. 2.

TO ILLUSTRATE DR. ROBERT GIBSON'S CASE OF KERATODERMIA BLENNORRHAGICA.

CLINICAL NOTES.

A CASE OF KERATODERMIA BLENNORRHAGICA.

ROBERT GIBSON, M.D.,
Hon. Dermatologist, Salford Royal Hospital; Hon. Assistant Physician, Manchester and Salford Hospital for Skin Diseases.

J. W—, aged 31 years, contracted gonorrhœa in 1913, for which he was treated and said to be cured. During the same year he was treated for rheumatism in the right leg for six weeks. He joined the army in September, 1914, and was invalided from France with iritis, for which he was treated eleven weeks, and returned to France August, 1915; was invalided in October, 1916, with heart trouble. He went to Egypt June, 1917, where he was in hospital from July, 1918, to December, 1918, suffering from rheumatism. He was eventually sent home and discharged the army March, 1919. He returned to his work as a carter, but was frequently under treatment for rheumatism until May 31st, 1922, when he was admitted to Salford Royal Hospital, under my colleague Dr. Ashby, suffering from acute articular rheumatism of the hands, feet and knees.

I was asked to see him in June for balanitis, and the above history was then discovered. Prostatic massage was ordered and the discharge examined. Mr. Jenkins reported a few pus-cells in the films: no definite organism to be found. Culture revealed a mass of saprophytic organisms. Recommended prostatic massage and irrigations. During the second week of July a number of small conical horny lesions developed on the little finger of the right hand and gradually spread to the dorsum of both hands and feet. Gonococcal vaccine was ordered in conjunction with the prostatic treatment. This treatment was at first followed by alleviation of the joint trouble, but the skin lesions progressed until they reached the size shown in the accompanying illustrations. The urethral discharge, which at first was very scanty, now increased in a marked degree, and never again lessened. The excrescences were removed by poulticing, but the base of the lesions showed a great tendency to form outgrowths.

The joint condition became much worse, and a gradual septicæmia developed, from which he eventually died in January, 1923. The Wassermann reaction was entirely negative and cultures from the blood were sterile.

HERPES ZOSTER AND VARICELLA.

A. C. ROXBURGH, M.D., M.R.C.P.,
Chief Assistant, Skin-Department, St. Bartholomew's Hospital.

In view of the controversy which exists as to the possibility of a relationship between these two diseases, it seems worth while adding two more to the number of cases already reported in which the two diseases have appeared to be associated.

On November 29th, 1922, I was asked by Dr. Malcolm Donaldson to see a married lady who had recently had a miscarriage. The day before I saw her she had developed a number of small scattered vesicles here and there on the trunk and limbs. The vesicles, each about 3 mm. in diameter, rose from healthy skin with no surrounding areola, and no preliminary macules or papules had been observed. The patient's temperature had risen to 101° F. on the day the vesicles first appeared, and subsequently reached 104° F. There were only about fifteen vesicles altogether, for the most part widely scattered, although there was a little group of three about the left angle of the mouth, and another of the same number about the position of the left saphenous opening.

Prof. F. R. Fraser, who had also seen the patient, and I were at first in some doubt about the diagnosis, but next day all doubts were set at rest, as the patient then had the typical eruption of varicella with macules, papules, and vesicles in process of eruption. The rash came out thereafter in three successive crops and in all respects behaved as a typical varicella.

The interest of the case lies in the fact that the patient's husband, sixteen days before, had had a typical attack of herpes zoster affecting the 6th, 7th and 8th intercostal spaces on the left side of the sternum, the herpetic vesicles appearing after three days of prodromal pain.

Neither the lady nor her husband had, so far as they knew, been exposed to infection with chickenpox. The husband had had chickenpox in childhood.

Another example of the association of the two diseases came to my notice some time ago in a family with which I am well acquainted, although I did not see the patients myself. In this case the cook of a household in Suffolk developed herpes zoster accompanied by a

good deal of pain about June 10th, 1921. A child, aged 2¼ years, staying in the house, developed varicella sixteen days later, on June 26th, although there was no other varicella in the neighbourhood at the time, and the child had been staying there for 4–5 weeks and so could not have been infected before arriving. The sister of this child, aged 3¼ years, was the next to develop the disease (about July 10th), although she was supposed to have had varicella before. Other cases followed, and in all there were five cases of varicella in the household—three children and two adults.

I am indebted to Dr. D. W. Ryder Richardson and Dr. E. Abdy Collins, of Saxmundham, for permission to publish the details of these latter cases.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

Meeting held on December 21st, 1922, Dr. H. G. Adamson, President of the Section, in the Chair.

Dr. J. H. Sequeira showed a case of *bullous eruption*. This patient was a boy, aged 3½ years; there was another child in the family, aged 13 months. The family history was unimportant. The child's general health was good; there was no evidence of visceral disease, but for the last six months there had been an eruption of bullæ. These came out singly and in groups, and they varied in size from that of a split pea to that of half a cob nut. They contained perfectly clear serum, and the base, at the onset, was free from erythema. Practically the whole surface was covered with groups of blebs. There was some irritation at night, but the child took its food well. The temperature was quite normal. There was slight eosinophilia of the blood, 10 per cent., but no eosinophils in the serum. At first the blebs were free from organisms, so far as cultures showed: later, however, they apparently developed *Staphylococcus epidermidis albus*. Following the example of the late Dr. Colcott Fox, he had entitled the case one of "bullous eruption."

The question whether this was pemphigus or dermatitis herpetiformis was purely one of nomenclature, or of what one understood by those terms. Taking the term "pemphigus" to mean a bullous eruption where the blebs came out on a clear skin and where the disease was not essentially

polymorphous, this should be classed as pemphigus. From the cases seen in the past he thought this case would do well, and most there would agree it was a condition which usually reacted well to arsenic.

Dr. Graham Little said this case revived an old discussion. He had always urged that the division of bullous eruptions into two classes, "pemphigus" and "dermatitis herpetiformis," was premature, and that the group should be recast. He did not see why the name "dermatitis herpetiformis" should not be applied to this case, as it seemed to fulfil many of the criteria of that condition. He had looked through his own cases, and found he seldom recorded having seen pemphigus, whereas Dr. Radcliffe-Crocker appeared as seldom to have seen dermatitis herpetiformis, though no doubt both he and Crocker had seen the same types of cases and labelled them differently. Therefore Dr. Sequeira acted wisely in calling this a bullous eruption; it was admittedly either dermatitis herpetiformis or pemphigus.

Dr. H. G. Adamson, (President), showed a *case for diagnosis.* The patient, a young woman was referred to him some months ago by Dr. G. A. Hooton, of Durban, South Africa. She lived on a farm in a village about seventy miles from Durban, and before this had worked for some years in a general store where she served both Europeans and natives. During the past five years there had appeared upon her face and other parts deep-red mahogany-coloured plaques, the nature of which was doubtful. Dr. Hooton was inclined to regard them as lupus erythematosus or lupus vulgaris: others who had seen them had diagnosed discoid, superficial rodent ulcer or basal-cell epithelioma of the type of which they had seen several examples lately. When he first saw the patient he hesitated as to the diagnosis of lupus vulgaris, to which the plaques certainly bore a close resemblance, and came to the conclusion that they were the lesions of leprosy of the macular variety—a diagnosis which he was interested to find had also suggested itself to Dr. Castellani, who had seen the patient that afternoon.

The distribution of the lesions was as follows: Eight on the face, viz. one at the outer third of each eyebrow, three on the nose, one on the upper lip, one over the lower jaw on left side and one in front of the left ear; three on the scalp; one on the front of the neck, and one on the left forearm. They varied in size from $\frac{1}{4}$ in. to $1\frac{1}{2}$ in. in diameter. They were irregularly rounded, very sharply margined, with a smooth surface not raised above the level of the skin, and semi-translucent aspect not unlike that of a superficial lupus infiltration. They differed, however, from lupus patches in the superficial infiltration being uniform and not nodular and in their curious deep mahogany colour. Some of the patches, notably

that one in front of the left ear, showed pale leucodermic-like areas as though part of the infiltration had disappeared, leaving a fine atrophy. One of the lesions, that on the upper lip, had a slightly raised margin which gave it somewhat the appearance of a rodent ulcer, and on very close inspection the same narrow raised margin could be seen faintly indicated in the other lesions. The patches on the scalp showed a central part where there had apparently been ulceration which had left scarring and destruction of the hair-follicles. All the patches seemed to be hypersensitive to the touch of a needle, compared with the surrounding skin. The patient had no other signs or definite symptoms of leprosy. She had complained for some months of feeling very tired and ill and of pains across the chest.

In order to aid the diagnosis, serum from a scraping of the surface of a lesion was examined for leprosy bacillus, but with negative result. A piece of the plaque on the forearm was removed for microscopical examination. It showed neither a basal-cell epithelioma nor a granuloma, but, in his opinion, the structure of a xanthoma. The epidermis was intact; in the corium from immediately beneath the epidermis to half-way towards the subcutaneous fat there was a very sharply circumscribed cell infiltration made up apparently entirely of so-called "epithelioid" cells, or oval cell nuclei, separated from one another by translucent finely granular masses which surrounded each cell or nucleus. Some of the "nuclei" were rounded, but these were probably oval nuclei in cross section and not lymphocytes. There were no outlying lymphocytic "muffs" such as one saw around the main cell infiltration of a granuloma, and outside the sharply margined infiltration the corium appeared normal. Dr. Barber, who had also made a microscopical preparation from another plaque, suggested that the appearances were those of a "sarcoid," but he was still inclined to regard them as those of a xanthoma in spite of the fact that the clinical features did not suggest a xanthoma. There was no sugar in the urine.

Dr. A. Whitfield agreed that this was a very difficult case about which to be sure. He had been wondering whether it was possible always to diagnose leprosy correctly by the presence of bacilli in the skin in the anæsthetic cases. The bacillus was, he thought, found in the nerve trunk in them. The lesion exhibited under the microscope did not suggest an inflammatory condition: yet in the absence of special staining he did not feel convinced it was xanthoma. The nearest condition which the specimen suggested to him was neurofibromatosis, but that was so far removed from the clinical appearance that it must be a mere accidental resemblance.

Dr. F. Parkes Weber said that five years ago he showed a patient as a case of some peculiar kind of xanthoma on the legs.* That patient had been a long time in England. After being exhibited, the case turned out to be one of leprosy.† It was interesting that Dr. Adamson's first thought was that the present case was one of leprosy.

Dr. Arthur Powell said he had seen a good deal of leprosy, especially in Bombay, where he was inspector of leprosy for a good many years, and visitor to an asylum of 450 beds, and this present case did not in the least suggest leprosy to him. In the nervous form of leprosy, it was almost the rule to fail to find the bacilli in the patches, but not uncommon to find them in the patient's nasal secretion when the nasal cavity showed no obvious lesion with the speculum.

Mr. J. E. R. McDonagh said he had examined the section from this case, and was struck by the sharply circumscribed character of the infiltration and the absence of polymorphonuclear leucocytes. The infiltration was made up, in the main, of endothelial cells, and the predominating leucocyte was the lymphocyte. The capillaries showed a general thickening. The histological picture reminded him more of that produced by a slow-growing coccidial protozoon than by anything else. It might be possible to discover the infecting agent if the section was stained with pyronin and methyl-green and examined with an oil-immersion lens.

Dr. S. E. Dore showed a *case for diagnosis*. The patient, a girl, aged 18 years, was shown for a peculiar condition of the right breast of five years' duration. There was no history of any preceding pathological condition of the breast, with the exception of an abscess in infancy, and there appeared to have been no undue swelling or pressure dragging on the organ. The right breast was larger than the left, the swelling being more pronounced in the lower and inner quadrant. The skin in this region was puckered from atrophy and presented numerous small brownish infiltrations in its substance, grouped in a horizontal direction, with minute slightly raised papular excrescences on the surface. There was no definite linear arrangement as would be expected in lineæ atrophicæ.

Dr. F. Parkes Weber regarded this as a case of so-called linear atrophy (striæ atrophicæ) of the skin, analogous to that not rarely seen about the shoulders, axillæ, or hips of rapidly growing adolescents. A determining local cause in the present case could probably be found in the manner of dressing, some garment or support keeping up a relative skin-tension below the large right breast. The exact nature of the right-sided mammary hypertrophy in the present case was of no special significance in regard to the cutaneous condition; which latter was due, as in all cases, to relative overstretching of the skin, combined with active (normal or pathological) growth, or œdema or other swelling, of the parts beneath the cutis. The striæ atrophicæ were the result of

* *Proc. Roy. Soc. Med*, 1917, x (Sect. Derm.), p. 164.

† *Ibid.*, 1920, xiii (Sect. Derm.), p. 12.

separation or cleavage of the cutis, as a method of adaptation; and some subjects were apparently specially predisposed to such striæ.*

Major G. Petit, R.A.M.C. showed a case of *lymphangioma circumscriptum of tongue.* The patient, a young man, was convinced that this condition of the tongue only started in August, 1920, while he was in hospital with amœbic dysentery in Constantinople, and that it attained its present size in three months. At first the tongue was so sore that he had to take his food cold. Recently the soreness had returned. It was thought to be a sequel left from the dysentery. Lieutenant-Colonel Perry, of the Royal Army Medical College, diagnosed lymphangioma circumscriptum, and he had brought the case hoping to receive suggestions as to treatment.

Clinically the lesion involved most of the right half of the tongue, extending down to the floor of the mouth; the tip of the tongue was not involved. The growth was typical, consisting of thick-walled, pea-sized, opalescent frog-spawn-like vesicles, with small areas of telangiectasis scattered through it.

Dr. A. M. H. Gray said he thought there was only one thing to do in such a case as this, and that was to destroy the surface of the tongue by diathermy, or the cautery. Unless it was inflammatory, he did not think any X-ray or radium treatment would suffice. He had found extensive vascular nævi of the mucous membranes did very well when treated with liquid air.

Dr. H. G. Adamson (President) said he thought it questionable whether these lymphangiectases were always of nævoid character. If, as he believed, they were sometimes acquired inflammatory conditions there would be some prospect of doing good by means of X-ray treatment.

Dr. J. H. Sequeira expressed his agreement with Dr. Gray's suggested treatment. He would apply the diathermy in patches, each time under a general anæsthetic, as he had seen great œdema follow extensive diathermy in the buccal cavity. He would work round the edges first.

Dr. Graham Little said he had a case, which he had referred for treatment to Mr. Cumberbatch, of a remarkably vascular nævoid growth, occupying the whole of the right cheek and the mucosa in the mouth. The patient was aged 17 years, and she had been under his observation twelve years. Pyorrhœa was definitely present, and the offensiveness of the mouth rendered some measure imperative. He first tried freezing on the accessible parts, and for some time that seemed to be a success. But there was a re-growth. He then tried electrolysis under anæsthesia, and for a short time this succeeded. Two months ago Dr. Cumberbatch applied diathermy, and now there was a recurrence as bad as ever.

Dr. S. E. Dore said he had seen many vascular nævi of the mucous membranes do very well under radium, and he thought it might be suitable in this case.

Dr. Semon agreed with Dr. Gray, and thought that there could hardly be a more positive indication for the use of electro-coagulation by diathermy than an

* *Cf.* F. Parkes Weber, "Unilateral Striæ Atrophicæ," *Practitioner*, Lond., 1917, cix, p. 453.

intra-buccal lymphangioma, such as was present on the tongue in this case. These tumours were notoriously susceptible to infection, and if such occurred here—as was not unlikely in the reactive stage after radiotherapy—he thought angina or œdematous swelling of the larynx might occur, endanger the patient's life, and render a tracheotomy necessary. It had been found by laryngologists and others that diathermy was of the greatest value in destroying malignant growths in the mouth and throat. Lymph spaces were sealed up by coagulation, there was no hæmorrhage, no sepsis, and practically no pain—and little or no reaction, as the eschar separated.

Dr. E. G. Graham Little showed a case of *onychatrophia*. Patient, a girl, aged 10 years, began to develop these changes in the nails at the age of 5 years. One by one the affected fingers had lost their nails; apparently they had been absorbed, very much as in epidermolysis bullosa, but there was no other evidence of that disease there. The toes were quite normal.

Dr. H. G. Adamson (President) said he had seen a similar nail condition associated with acquired syphilis. This child might have congenital syphilis, and he suggested that a Wassermann test be carried out.

Dr. F. Parkes Weber suggested that this case was allied to cases of Raynaud's disease; and in Raynaud's disease one of the first things to find out was whether (by the Wassermann reaction or otherwise) any evidence of congenital or acquired syphilis could be obtained.

Dr. E. G. Graham Little showed a *section of excised pigmented mole showing early malignancy*. The section was taken from a flat congenital pigmented mole on the shoulder of a medical student in his class. He showed it to him a week or two ago, and said it was causing him some irritation. As there was continuous friction from the braces, Dr. Little suggested he should have it taken out. This was done. He was 24 years old. He had never seen a malignant change take place in a mole at anything like that age. The sections had been examined by Dr. E. H. Kettle, Pathologist to St. Mary's Hospital, who regards them as showing definite early malignancy.

Dr. H. C. Semon showed a case of *pigmented lesion for diagnosis*. Patient was a woman, aged 59 years, whom he saw for the first time a week ago. She had had this rapidly growing discoid, pigmented and papillomatous neoplasm on her right cheek for about a year. Clinically it was freely movable on the subcutaneous tissues, there were no palpable glands, and the microscopic evidence was not conclusive of malignancy. The section, which was open to inspection, shows numerous transverse and obliquely cut papillomata, and in the stroma surrounding them were thickly packed

masses of nævoid, epitheliomatous (or as has been suggested, "endotheliomatous") cells, containing melanin.*

Dr. J. H. Sequeira (discussing Dr. Semon's case) said he had a case of such a lesion on the hand, in one of his X-ray workers at the hospital, ten years ago. The growth was removed, and the man still remained well. If in this case it was intended to remove a piece for a section, it would be as well to remove the whole growth.

Dr. L. Savatard said that these patches of melanodermia frequently became malignant, and that they should be treated as liable to do so. He had had a case with the lesion in the same position as in this case, and he froze it. Apparently it cleared up. But the patient returned eighteen months afterwards with raised ulcerated and slightly pigmented recurrent growth. He excised it, and the pathologist's report was that it was sarcoma. It healed up quite satifactorily, and the patient did well. He had excised many pigmented moles, and tried, at different stages, but without success, to trace the start of malignancy. Dr. Graham Little's section shown to-day he did not consider malignant; it presented a pretty picture of a small pigmented nævus.

Dr. M. G. Hannay showed a case of *sclerodermia*. This patient, a man, aged 68 years, was suffering from a definite but mild degree of sclerodermia of the diffuse type involving the skin of the whole body with the exception of the extremities. The stiffness of the skin was first noticed in the neck about two years ago, and gradually extended. During the last two months there has been a definite improvement. This might be partly due to the administration of thyroid in small doses, and partly (latterly) to rest in hospital.

Through the courtesy of Dr. Izod Bennett, the patient was admitted to the Middlesex Hospital for the investigation of his basal metabolism, which was kindly undertaken by Dr. E. C. Dodds. While in hospital the temperature always remained subnormal; pulse ranged from 60 to 80. His basal metabolism was found to be 25 per cent. below normal. Excretion of sulphur during twenty-four hours showed no divergence from normal.

In addition to the sclerodermia, there were very numerous small tags of skin, some vascular nævi, and seborrhœic and pigmented warts. Although these symptoms did not constitute von Recklinghausen's disease, they might perhaps be suggestive of a partially developed case. It was, however, from the point of view of the sclerodermia that he was showing this patient.

Dr. F. Parkes Weber agreed that the case was one of generalised sclerodermia, but there did not seem sufficient ground for also diagnosing von Recklinghausen's disease.

* The growth was destroyed by diathermy under nitrous oxide anæsthesia in the following week.

CURRENT LITERATURE.

INFLAMMATIONS, ETC.

INFANTILE ECZEMA AND EXAMINATION OF THE STOOLS. Charles J. White. (*Arch. of Derm. and Syph.*, 1923, vii, p. 50.)

According to the writer, infantile eczema is more common in boy babies than girls in the proportion of 3 to 1. The disease is not present at birth, but seemed to appear at all ages, there being relatively few cases before the age of one month. The face is the favourite seat, and the next most common situation is the scalp. All the babies which formed the material for this contribution were breast fed, and in several instances the eczema developed soon after the cessation of nursing. Abnormal stools appeared to accompany every obstinate case, there being excessive fat in 60 per cent., excessive starch in 40 per cent., excessive sugar in 20 per cent., and excessive protein in 10 per cent. Rectification of the diet was followed by distinct improvement in the majority of the cases. J. M. H. M.

DERMATITIS VENENATA. V. Pardo-Castello. (*Arch. of Derm. and Syph.*, 1923, vii, p. 81.)

More than 40 species of plants have been found in the Antilles which produce dermatitis, varying from a mild erythema to a severe bullous condition, and in some cases with serious general disturbance. The dermatitis is caused by the latex of the plants or by their appendages, generally the hairs, which act not only mechanically but sometimes chemically, owing to the presence in them of an irritating acid oil. In certain cases the ingestion of the fruit of the plant seems to produce immunity. The tropical plants producing dermatitis are chiefly of the genera Anacardiaceæ, Leguminosæ, Euphorbiaceæ and Urticææ. J. M. H. M.

QUININE SICKNESS OF OCCUPATIONAL ORIGIN. Blamoutier and Joannon. (*Rev. d'Hyg.*, June, 1922, xliv, No. 6, pp. 521–532. Abs. *Journ. Ind. Hyg.*, January, 1922, p. 146.)

A man worked in a chemical establishment preparing the drug. After two weeks' employment, which included the handling of quinine bark in bulk and in powder and at the process in which quinine sulphate is produced, œdema of the eyelids was noted. Subsequently an itching erythematous eruption appeared on the face, anticubital spaces, genitalia, and the upper third of the inner aspects of the thighs. Here also was seen some œdema and later some vesicles developed on the face. The blood showed a positive Wassermann reaction, a leucocytosis (18,000) and an eosinophilia (23 per cent.).

The authors are of opinion that cases of this nature are not essentially different from those originating from the ingestion of quinine therapeutically administered. R. P. W.

A CASE OF MYCOSIS FUNGOIDES. Wellmann. (*Derm. Wochenschr.*, November 25th, 1922, Nr. 47, lxxv.)

This typical example of the disease followed the usual stages described for it.

There was a premycotic eczematous stage with the characteristic rounded areas of infiltration, abutting on islets of perfectly normal skin, marked itching, and the eventual development of soft tomato-sized growths, which had not ulcerated up to the time when patient was admitted.

Histologically the growths were composed of a multiform cellular structure—large round cells with deeply staining chromatin nucleus and small protoplasmic zone, like the elements of a lymphosarcoma.

Isolated groups of plasma and giant cells were also noted, and large lymphocytes were seen here and there.

According to this author it is the multiformity of cell type that renders the histological diagnosis of mycosis fungoides probable.

Before X-ray treatment (1 B. through 2 mm. filter to tumours, and ½ an unshielded B. dose to the erythema) was instituted, the blood-count was: Erythrocytes, 4 million; leucocytes, 25,600; hæmoglobin, 87 per cent.; polynuclears, 52 per cent.; large lymphocytes, 26 per cent.; small lymphocytes, 21 per cent.; eosinophiles 1 per cent. Three weeks after X-rays commenced: Erythrocytes, *nil*; leucocytes, 8200; polynuclears, 62 per cent.; large lymphocytes, 4 per cent.; small lymphocytes, 31 per cent.; eosinophiles, 3 per cent. Wassermann reaction negative.

The clinical results of the radiotherapy were, as usual, quite brilliant. All the tumours had disappeared within six weeks of commencing the treatment, and the erythema also had completely disappeared. H. S.

ON THE HISTO-PATHOLOGY OF MYCOSIS FUNGOIDES. G. Spremolla. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. v, p. 991.)

Careful examination of the tumours from a case of mycosis fungoides by all the modern methods showed a special granulomatous structure similar in appearance but fundamentally different from the lympho-granulomatosis of Sternberg-Paltauf. Towards the surface of the ulcerated tumours small cocci were found, which were probably due to secondary infection. R. C. L.

TWO CASES AND SOME CONSIDERATIONS ON THE PATHOLOGICAL ANATOMY AND PATHOGENESIS OF GENERALISED ARGYRIA. G. Maranon. (*Ann. Derm. et Syph.*, 1923, VIe série, iv, No. 1, p. 35.)

Argyria may be local or generalised. Both forms may be produced by occupation (jewellers, silver-nitrate packers, etc.) or by medicinal treatment with silver preparations. As examples of the localised form may be cited the bluish-grey patches on the hands, forearms, and chin of jewellers, and on the mucous membranes of the tongue, pharynx, nose and urethra, or on the skin, following the local treatment of ulcers, gonorrhœa, leucoplakia, etc., with silver nitrate or argyrol. The generalised form results from the absorption of silver or its salts; thus jewellers and others who work with the metal may carry particles of it to the mouth with food or with cigarettes, or may breathe air charged with minute metallic particles, and at one time silver nitrate was frequently given, usually in the form of pills, for diseases of the nervous system, *e.g.* epilepsy, tabes dorsalis, or in solution for gastric ulcer. Lochte has published a case produced by twelve injections of silver-salvarsan. Although, as a rule, large quantities of silver have to be absorbed before typical argyria is seen, this is not always so; there

must be, therefore, some other predisposing factor or factors which favour precipitation of the metal in the tissues. The sites of election for such precipitation are as follows:

(1) The dermis (never the epidermis) between the elastic fibres, in the connective tissue of the sebaceous and sweat glands, in the muscle-fibres of the medium-sized arteries and the veins, and in the adventitia of the arterioles.

(2) The mucous membrane and submucosa of the pharynx, stomach, large intestine, and, less frequently, the small intestine.

(3) The connective tissue of the liver, the glomeruli of the kidneys, the mesenteric glands, and the choroid plexus.

The pigmentation is usually first seen as a steel-grey line along the gum-margins, and on the free edges of the eyelids, and around the nails. Then follows a gradually increasing, diffuse, metallic-blue discoloration of the skin of the parts exposed to light, which is more intense in blondes than in dark-complexioned persons. The author gives very clearly the differential diagnosis between argyria and Addison's disease—in both the cases described by him the latter condition had been diagnosed—and he points out that the two should never be confused.

Of his cases the first, a male, had been given silver nitrate pills for a suspected gastric ulcer, but he took not more than two per diem, and that for a period of two or three weeks only; the discoloration of his skin appeared a few months later.

The second patient, a female, had been given a very dilute solution of silver nitrate for gastric pain. A biopsy was made, and part of the excised skin was tested chemically for silver with positive result; the rest was examined histologically. The lower layers of the epidermis were deeply pigmented with melanin, and in the dermal structures were seen the silver particles. Three figures illustrating the microscopical appearances are given. H. W. B.

THE RESISTANCE OF HAIR TO CERTAIN SUPPOSED GROWTH STIMULANTS. Mildred Trotter. (*Arch. of Derm. and Syph.*, 1923, vii, p. 93.)

The object of this paper is to refute the popular belief that hair growth is readily influenced by such external factors as cutting or shaving the hair, greasy applications and sunburn.

The normal rate of growth was first estimated in hairs from different regions. It was found that the weekly average growth of hairs on the axillæ was 2·9 mm.; at the vertex of the head 2·7 mm.; on the leg just below the knee 1·6 mm., and on the outer side of the forearm 1·5 mm.

It was found that the rate of growth of the hair in different regions of the body corresponded directly with the thickness of the hair.

Greasy applications were first experimented with. Petrolatum was rubbed freely into the front of one thigh in four women twice a week for a period of eight months, the other thigh being used as a control. At the end of the period two symmetrical lesions in the thighs were carefully compared by three observers, and no differences in the hair growth were detected. This experiment indicated that the prolonged use of petrolatum does not cause the short downy hairs to either become longer or coarser. Similar results were found in connection with the eyebrows.

Experiments on similar lines were carried out with shaving, and it was found that the shaving did not cause any increase in the rate of growth, nor in the type of hair which grew.

With regard to the effect of actinic rays, it was found that the rays accelerated the hair development during the growing period, perhaps causing it to reach its final length at an earlier date, but that they had no effect on the ultimate amount of hair produced. J. M. H. M.

TAR MELANOSIS. A. Kissmeyer. (*Arch. f. Derm. u. Syph.*, Bd. cxl, Heft 3, p. 357.)

A case of tar melanosis is reported in a female, aged 26 years, who had for two years been working in an asphalte factory. The pigmentation was most marked on the prominent parts of the face, chin and neck. Beyond the skin affection no abnormality was found. An account is given of the morbid anatomical examination. The theory is put forward (based on Bloch's "dopa" researches) of a purely *chemical action* of the oxydase—present in the epidermal cells—upon some derivative of the benzol ring bodies contained in crude tar. This theory is further elaborated in a tentative explanation of the pigment formation occurring in Addison's disease and in ochronosis. W. J. O.

A CASE OF ACNITIS. Luigi Bussalai. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. i, p. 40.)

A typical case of acnitis is described with photographs of sections from the skin showing nodules with giant-cells. Guinea-pig inoculations with tissue from the lesions were negative, and no tubercle bacilli were found microscopically, but the patient showed slight rises of temperature, an apical lesion in the right lung, and gave a positive reaction to tuberculin. A list of previously published cases is also given. R. C. L.

A CASE OF BENIGN MILIARY LUPOID (BOECK). G. Segré. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 646.)

The case described was a papulo-nodular tuberculide on the face of a man, aged 39 years. The cuti-reaction to tuberculin was negative, as also the search for tubercle bacilli and inoculation of animals. Microscopically the lesions showed a typical tuberculous granuloma. The Wassermann was negative. The lesions healed up spontaneously after about three months. The author lays stress on the rarity of this condition in Italy. Photographs of the patient and of sections of the lesions are given. R. C. L.

AUTO-VACCINATION THERAPY IN LEPROSY. R. Porcelli. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 719.)

Cases of leprosy were treated with a vaccine made according to the method of Gougerot and Winkelried, by macerating leprous nodules in a mortar and making an emulsion containing the leprosy bacillus. It was reckoned that each c.c. of this emulsion contained about two million bacilli. Subcutaneous and intramuscular injections were given in doses of 1–5 c.c. at intervals of 6–12 days. Two cases of nodular leprosy treated in this way, each with twelve injections, showed a slight improvement. No local reaction was produced. Similar

doubtful results were obtained in two other cases with intravenous injections (25–100 millions) of an autogenous vaccine. Later a vaccine was prepared by treating the leprous nodules after maceration with a 5 per cent. antiformin solution and then centrifuging. By this means an abundant, almost pure culture of the bacillus was obtained and made into a vaccine with roughly 500 million per c.c. After several subcutaneous injections (500–1000 million), followed by a slight local and general reaction, there was a marked improvement in two cases treated. Other cases are still under treatment by this method.

R. C. L.

A STATISTICAL RECORD UP TO 1921 AND PROPHYLACTIC CONSIDERATION OF LEPROSY. A. Serra. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. iii, p. 767.)

The number of cases of leprosy in Italy within recent years is given. Isolation is recommended as the best way to prevent the spread of the disease in all countries where it exists, either diffusely or in localised areas. Compulsory notification, supervision and isolation, as practised in Norway, should be insisted on. For Italy he recommends five colonies: one in north Italy, one in central and one in lower Italy, one in Sicily and one in Sardinia. R. C. L.

TWO CASES OF PAPULO-NECROTIC DIABETIDES. L. Tommasi. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1921, fasc. v, p. 478.)

Two similar cases are described, both in women with diabetes. The eruption affected both lower limbs in one case, and one lower limb and corresponding nates in the other case. It was papular at first with purulent and necrotic centre later on, and was distributed more or less in lines down the limb. Biopsies were made and animals inoculated so as to exclude tuberculides. The animal inoculations were negative, and microscopically no tubercle bacilli were found and granulomatous tissue was also absent, only a small-celled infiltration being present. Tommasi thinks the eruption was due to the glycosuria. Photographs of the eruption are given and a coloured drawing of the histology of the condition. R. C. L.

SYPHILIS.

CONTRIBUTORY FACTORS IN POST-ARSPHENAMIN DERMATITIS. John H. Stokes and Edward P. Cathcart. (*Arch. of Derm. and Syph.*, 1923, vii, p. 14.)

In the experience of the writers the cutaneous reactions of arsphenamin in general are not dependent on the amount of the drug administered, and show a tendency to occur early rather than late in the course of its administration. They appear to have no definite connection with the administration of mercury, nor do they seem dependent on any real abnormality, such as might be due to the mercury.

In a great proportion of their cases they found evidence that chronic focal and acute prodromal or intercurrent infections were connected with the development of arsphenamin cutaneous reaction, and that the severity of the reactions was in direct relation to the extent of the infective factor. In one case they have

witnessed the immediate involution of a severe post-arsphenamin dermatitis on the total exacerbation of a septic focus.

The septic foci consisted of septic tonsils or defective teeth. The writers point out the importance of disposing of any focus of infection before the treatment is commenced. Should it be detected when the cutaneous reaction has developed, they consider it unwise to interfere with the focus until a rest interval between courses of treatment. J. M. H. M.

TREATMENT OF ARSPHENAMIN DERMATITIS AND CERTAIN OTHER METALLIC POISONINGS. William L. McBride and Charles C. Dennie. (*Arch. of Derm. and Syph.*, 1923, vii, p. 63.)

According to the writers, sodium thiosulphate given intravenously, and by the mouth, rapidly shortens the course of arsenical dermatitis, and is also a successful neutralising agent for acute and chronic mercurial poisoning. It is best given intravenously, and in its pure form is non-toxic up to 2 grm. doses. The initial dose given was ·3 grm., and this was gradually increased on successive days. The writers concur with the general belief that certain conditions which impair the liver or kidneys are predisposing factors in the production of arsphenamin dermatitis. J. M. H. M.

A CASE OF FATAL SALVARSAN PURPURA. F. Callomon. (*Derm. Wochenschr.*, December 9th, 1922, Nr. 49, lxxv.)

A man, aged 25 years, with early secondary eruption and a strongly positive Wassermann reaction, was given the following treatment: March 26th—neosalvarsan, ·15 grm.; mercury salicylate, ·05; March 29th—mercury salicylate, ·1; April 3rd—neosalvarsan, ·3; mercury salicylate, ·15. On the same day patient reported the appearance of small punctiform hæmorrhages on legs, thighs, shoulders and cheeks, and by the 6th inst. these punctiform lesions had enlarged and coalesced to form extravasations on the skin, and petechiæ of various sizes on the mucous membranes of mouth and throat. There was also hæmaturia.

April 7th: Increased hæmorrhages, with dyspnœa. Liver and spleen not palpable. Severe submucous hæmorrhage behind post-pharyngeal wall.

Blood examination revealed a few nucleated red corpuscles and erythrocytes. No poikilocytosis or malarial parasites.

April 8th: Liver palpable. New hæmorrhages, retinal (L.) especially. Sudden death later in the day.

The post-mortem examination revealed hæmorrhages everywhere in the subcutaneous tissues, and in the serous cavities. Death appeared to have been directly caused by pulmonary asphyxiation due to bleeding into bronchi.

Microscopically the hæmorrhages were nowhere accompanied by evidence of inflammation. They were, in fact, a direct "diapedesis sanguinis."

The author admits to difficulty in attempting to classify this unusual case. According to Leder, *M. Kl.*, 1922, Nr. 48, there are two types of salvarsan purpura:

A. One with severe changes in the blood picture, loss of coagulation power, and pathological changes in red marrow—a triad which is attributed to the benzole group.

B. The other exhibiting angiopathic or anaphylactoid symptoms, with extensive damage to endothelium of capillaries.

Callomon's case would seem to show that neosalvarsan may produce mixed types, according to the above classification.

The fact that after only two small doses of the drug (·15 and ·3 grm.), at an interval of 8 days between the doses, argues in favour of an unusual idiosyncrasy to arsenic derivatives on the part of the patient. The batch number, which had been registered at the time of the injections, proved entirely innocent in other cases. H. S.

PREPARATIONS OF BISMUTH IN THE TREATMENT OF SYPHILIS. A. Pasini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. iii, p. 814.)

Sodium and potassium bismuth tartarate were used (1) as an oily suspension (trepol) and (2) in watery solution (luatol) in thirty-one cases of syphilis in all stages. 20–30 cgrm. were given every two to three days from ten to twelve times. Usually spirochætes disappeared from the lesions after the first or second injection. The lesions healed rapidly, but after eight to ten injections the Wassermann usually remained positive. There was sometimes pain at the seat of injection. The most serious difficulty was stomatitis, which might go on to a severe ulcerative and gangrenous condition of the gums. Although the number of cases treated is small, the author thinks that bismuth and its derivatives have a definite specific action in syphilis. They seem to be more active against the spirochæte than mercury, but slower in causing an absorption of the infiltration. The bismuth preparations are less active than arsenobenzol. The author thinks it is a useful drug where there is an intolerance of mercury or arsenic.

R. C. L.

ON THE NEW METHOD OF TREATMENT OF SYPHILIS WITH SALTS OF BISMUTH. A. de Bella. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. iii, p. 827.)

The preparations used were sodium and potassium bismuth tartarate. Eight cases so treated are reported. The results were constant, complete, but not conspicuously rapid. The action on the Wassermann reaction was good in one case only. A good deal of pain was complained of at the seat of injection and sometimes also swelling. General disturbances, such as headache and rise of temperature, were seen only after the first injections. Stomatitis was not constant, but inconveniently frequent. The author thinks the remedy is worthy of further trial. R. C. L.

BISMUTH TARTARATE IN THE TREATMENT OF SYPHILIS. G. Define. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. iii, p. 834.)

Eight cases of syphilis in different stages were treated. In none was there any reaction at the seat of injection, and in one case stomatitis developed. In three out of four cases tested the Wassermann reaction was turned from positive to negative. The author found that this drug has considerable advantages in the treatment of syphilis, but in one case of general paralysis the result was absolutely *nil*. R. C. L.

THE VALUE OF BISMUTH IN THE TREATMENT OF SYPHILIS. A. Radaeli. (*Giorn. Ital. d. Mal. Ven. e. della Pelle*, 1922, fasc. v, p. 1043.)

The author used trepol (tartaro-bismuthate of sodium and potassium in oily

suspension) and luatol (tartaro-bismuthate of sodium and potassium in aqueous solution). He found that with these preparations skin and mucous membrane specific eruptions are rapidly influenced. Brilliant results were obtained, especially in cases with papulo-pustular and diffuse lenticulo-papular eruptions which had resisted arseno-benzol and mercury. The spirochætes disappeared from the lesions fairly quickly, glandular swellings diminished and the patients' general condition improved. The Wassermann reaction was not constantly influenced. Stomatitis is the most frequent complication, and occurred more frequently with insoluble than with soluble preparations. Renal changes may occur, producing albuminuria, but this usually rapidly disappears when the treatment is stopped. The author thinks the drug merits a trial, and thinks that probably new preparations of bismuth might give better results. A full bibliography is given.

R. C. L.

A RARE SITUATION FOR A PRIMARY SORE. G. Nardi. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. i, p. 58.)

In this case the primary sore was situated on the scalp. The lesion followed a bite on the scalp, and this is recorded on account of the rarity of this situation. Statistics of previously recorded cases are given. R. C. L.

A PRIMARY SORE ON THE AURICLE. L. Morini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 101.)

A primary sore developed on the left auricle of a man, aged 24 years. The lesion began as a small furuncle in that situation and infection probably took place by kissing before the boil had completely healed. The diagnosis was confirmed by finding the *Spirochæta pallida*. The glands in the parotid region were enlarged and a secondary rash appeared on the body. The lesions were cured by neosalvarsan mixed with cyarsal and intravenous injections of calomel. Reference is also made to all the previous cases of primary sores on the auricle.

R. C. L.

A CASE OF MULTIPLE CUTANEOUS TUBERCULOUS GUMMATA SIMULATING, AT FIRST, THE ERUPTION OF ERYTHEMA NODOSUM. P. Caldarola. (*Giorn. Ital. d Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 654.)

The patient was a female, aged 15 years, who, whilst in apparently good health otherwise, developed suddenly rheumatoid pains, accompanied by fever and a nodular eruption localised chiefly to the lower limbs but with a few lesions on the face and forearms. The nodules were the size of a hazel-nut and were bluish-red in colour and fairly hard. Some were dermic, others hypodermic. There was also a tenosynovitis of the tendo Achillis of left leg, and erythematous and erythemato-hæmorrhagic lesions of the distal ends of the lower extremities. The chest showed a tuberculous lesion of right lung. Some of the skin-lesions became of a bluish colour and were slowly absorbed, but many of them softened, producing tuberculous ulcers. The cutaneous tuberculin test was positive. Microscopically the lesions showed a tuberculous structure, and inoculations of guinea-pigs were positive. The author discusses the relation of such cases to true erythema nodosum occurring in tuberculous patients.

R. C. L.

INTRANASAL PRIMARY SYPHILIS. P. Ramognini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. iii, p. 789.)

Four cases of this condition are recorded. The lesion usually appears as a small swelling in the nasal cavity, ulcerated on the top, and the base of the ulcer covered with an adherent diphtheritic-like exudate. There is usually pain radiating up to the orbit and head. A mucous or hæmorrhagic discharge is usually present. There is considerable swelling of the corresponding cheek and ala nasi. There is considerable swelling of the glands below the jaw, also pre-auricular and parotid lymphatic glands. The sore usually runs a longer course than the ordinary genital and most extra-genital chancres, and usually by the time it is diagnosed secondary symptoms are already present. The exact mode of infection is not always traceable, the commonest probably being by introducing an infected finger into the nose. A full list of previously recorded cases is given. R. C. L.

THE DR. SOFIE A. NORDHOFF-JUNG CANCER RESEARCH PRIZE.

Dr. Sofie A. Nordhoff-Jung, of Washington, District of Columbia, United States of America, has founded an annual prize of five hundred dollars, bearing the title of "The Sofie A. Nordhoff-Jung Cancer Research Prize." This prize is destined for the encouragement of researches in the ætiology, prevention and treatment of cancer. It will be awarded by a commission, composed of members of the University of Munich, Bavaria, and be granted for the first time in December in the year 1923. The commission consists of Profs. Borst, Doederlein and Sauerbruch, with Prof. von Romberg as chairman. This body is empowered to elect successors. The award will be made as a recognition of the most conspicuous work in the world literature bearing on cancer research, done at a time antecedent to the allotment of the award. Though the prize will not be awarded on a competitive basis, the commission invites all research workers in cancer to submit literature on this subject.

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THE BRITISH JOURNAL

OF

DERMATOLOGY AND SYPHILIS

MAY, 1923.

THE MYCOTIC TYPE OF BROMODERMIA AND IODODERMIA: FACIAL, PHARYNGEAL, AND INTRA-ORAL ŒDEMA, AND SWELLING OF SALIVARY AND THYROID GLANDS IN CASES OF IDIOSYNCRASY TOWARDS IODIDES.

F. PARKES WEBER, M.A., M.D., F.R.C.P.

(A) The Mycotic Type of Bromodermia and Iododermia.

The term "bromodermia" is not here used (by analogy with the word "bromidrosis") to signify a condition of badly smelling skin, but to signify any of various disorders of the skin consequent on the taking of bromides by normal persons or by those with a special idiosyncrasy towards bromides. Few drug-eruptions are as remarkable and as liable to give rise to grave errors in diagnosis as the "mycotic," "granulomatous," "fungating," "vegetating," "sarcoid," or "frambœsial" type of eruption due to the ingestion of bromides or iodides. Such eruptions have been termed *bromodermia*, or *iododermia tuberosum* (or *nodosum*) *fungoides*. A patient may be treated with potassium iodide for suspected syphilis when in reality he has not syphilis, but perhaps a tendency to some kind of exudative erythema with a special idiosyncrasy towards iodides. If under such circumstances a mycotic iododermia arises it may be mistaken for a florid syphilitic condition, and still larger doses of iodide may be administered, with grave results.

Such a chain of events may constitute a kind of trap or pitfall into which the doctor at first nearly stumbles, and then by a sudden wrong movement completely falls. An excellent example of "tubercular iodism" in a man, aged 30 years, simulating gumma of the eyelid (syphilitic granuloma), was described by Sydney Stephenson in

1914.* The confusion in diagnosis may be rendered more dangerous by this type of eruption sometimes becoming worse for some days following cessation of the drug-treatment. Some cases have been confused with mycosis (granuloma) fungoides or with sarcoma. O. Rosenthal described a case of granulomata closely resembling mycosis fungoides, but really due to the ingestion of potassium iodide. Sir Jonathan Hutchison, at the Dermatological Society of London in December, 1893, showed a drawing of iodide "sarcomata" in an old feeble man in an infirmary, who had been given potassium iodide for chronic rheumatoid troubles. The iodide was persisted in as the iodide eruption had been then mistaken for syphilis.† In 1917 W. K. Sibley showed a case of bromide eruption in which the condition first of all suggested a blastomycosis cutis.‡ So it did in part in the case of an infant recorded in 1917 by M. Scholtz.§

In one case, in a patient with scars of former tuberculous bone disease, I thought at first that a scrofulodermia had followed bromide treatment, but to that case I will further on return. In another case (elsewhere) it was suggested that the eruption was scrofulous, and that it had been started by giving the patient bromide, but a distinguished dermatologist refused to accept the double ætiology. I cannot help thinking, however, that in a scrofulo-tuberculous subject an idiosyncrasy towards iodides or bromides may be regarded as being possibly due to the scrofulo-tuberculous condition. Occasionally chronic renal disease, and probably chronic alcoholism, cachexia, old age and general feebleness may be partly responsible for the drug idiosyncrasy.

In regard to treatment, I certainly agree that the administration of small doses of arsenic may to some extent oppose the undesired action of bromides or iodides. K. Hubschmann has recently recommended calcium therapy, as he has found that in such cases the calcium content of the blood is diminished.‖

Unna¶ thought that in iodine dermatoses the resistance of the skin

* S. Stephenson, *Medical Press*, London, 1914, cxlix, p. 115.

† See *Brit. Journ. Derm.*, 1907, xix, p. 441.

‡ W. K. Sibley, *Proc. Roy. Soc. Med., Derm. Sect.*, 1917–1918, xi, p. 32.

§ M. Scholtz, *Urol. and Cut. Rev.*, 1917, xxi, p. 203.

‖ Hubschmann, *Ceská Dermatologia*, 1922, iii, p. 280; abstract in *Brit. Journ. Derm. and Syph.*, 1923, xxxv, p. 76.

¶ Unna, *Histopathology of Diseases of the Skin*, English translation, 1896, p. 107.

to parasitic infection was diminished. Recently U. J. Wile, C. S. Wright and N. R. Smith,* as the result of their experimental observations on iodide and bromide exanthems, conclude that the pustules of iodide and bromide acne are not sterile, but that the bacteria present are probably due to secondary contamination. They find also that iodide and bromide are not present in the purulent material from the acneiform lesions, and that the local phenomena of iododermia and bromodermia are not explicable on simple bacterial or chemical grounds, but are probably explained as due to a complex biochemical reaction.

I will now refer to a few illustrative cases :

Case 1.—An excellent example of the mycotic type of bromodermia in the

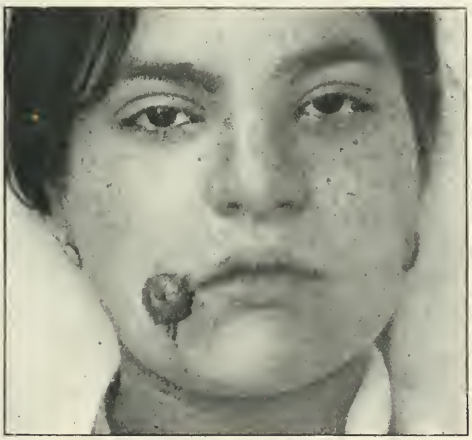

Fig. 1.—Granulomatous bromodermia. Case 1.

case of a Hebrew girl (M. S—), aged 15 years, who had been treated with bromides for hysterical symptoms. The scalp, the most affected part, presented raised patches of granulation-tissue tending to become covered with crusts of dried discharge. There were elevated, mostly circular plaques of various sizes on the face and extremities, and one on the trunk. The accompanying illustration (Fig. 1) shows a nodule on the patient's face. She was slightly anæmic and had depressed scars from old tuberculous bone disease on both feet, but otherwise appeared healthy. The case was shown at the old Dermatological Society of London on January 11th, 1905.† The eruption began to appear about

* Wile, Wright and Smith, "A Preliminary Study of the Experimental Aspects of Iodide and Bromide Exanthems." *Arch. of Derm. and Syph.*, 1922, vi, p. 529.

† *Brit. Journ. Derm.*, 1905, xvii, p. 63.

December 12th, 1904, four days after the commencement of the treatment with mixed bromides (37½ gr. per diem). I saw the patient first on December 22nd, when the bromides were discontinued, but the bromodermia continued to get worse for some time. Small doses of arsenic were employed. On January 26th I noted that the granulomatous growths appeared to be shrivelling. They were covered by crusts of epidermis and sebaceous material into which the "sprouting" (fungating) papillæ projected, so that when the (sebaceous-like) crusts were removed bleeding took place from the torn papillary blood-vessels. By February 20th the eruption on the head had practically gone, leaving a certain amount of scarring and discoloration.

Case 2.—The patient (Mrs. P. R—), aged 46 years, was admitted to hospital under my care on May 8th, 1922, with scattered purulent granulomatous lesions on the lower extremities (Fig. 2) and to a less extent on the upper extremities, but practically none on the trunk, neck, face or scalp. The cutaneous lesions mostly commenced as minute pustules or as groups of minute pustules on raised red bases. The patient said that she had been previously an in-patient (March,

1916) for a similar eruption, and the case had apparently then been diagnosed as a form of pemphigus. She had recovered under arsenical treatment. On the present occasion (1922), however, the lesions did not commence as vesicles or bullæ, and were evidently no form of pemphigus vegetans. The axillæ and groins were quite free from vegetating lesions, and the mucous membrane of the lips, cheek and mouth was not affected. The history pointed to the present attack being due to medication with mixed bromides (in the form of Erlenmeyer's mixture, 15 gr. of mixed bromides, three times daily). This had been prescribed in the out-patient department for neurotic and dyspeptic symptoms on February 27th and again on March 20th. The eruption had commenced two or three weeks before admission. Arsenical treatment was commenced immediately on admission (May 8th, 1922), but was left off on May 13th. For one or two days there was pyrexia.

On May 18th the cutaneous lesions were already rapidly diminishing. I told the patient that it was very important to make certain that the lesions were

really due to bromide treatment, so that in that case she could warn any doctors (whom she might consult for her neurotic complaints) that she had an idiosyncrasy towards bromides. If she did not warn them she would almost certainly be given bromides again. Her previous attack (1916) had been probably likewise due to bromide medication.

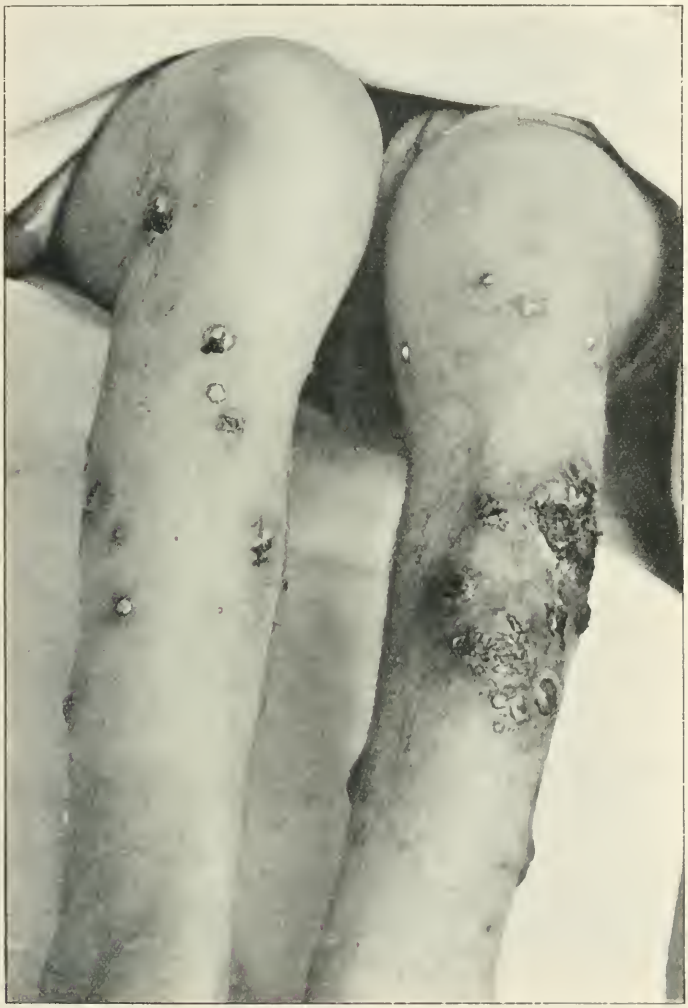

FIG. 2.—Granulomatous bromodermia. Case 2.

Accordingly, with the patient's consent, she was again, on May 18th, ordered 15 gr. of the mixed bromides (Erlenmeyer's mixture) three times daily. On May 22nd it appeared that the cutaneous lesions were still further drying up and disappearing, but on May 25th (seven days after again commencing to take

the bromides) fresh purulent lesions were appearing on the upper and lower extremities. Many of the new (commencing) lesions consisted in a few closely grouped or confluent pustules on a single raised red base. The bromide medication was immediately discontinued. The cutaneous lesions after that at first seemed to increase, but on May 28th they were commencing to diminish and

FIG. 3.—Granulomatous iododermia. Case 4.

dry up. It was a considerable time, however, before the condition, which was thus proved to be due to the bromides—a form of "granulomatous bromodermia"—completely healed up. For part of the time she was treated with calcium lactate (15 gr. three times daily) and Fowler's solution (3 min., in water, after meals, thrice daily). She left the hospital on July 5th.

Case 3.—On September 25th, 1922, about the time of the recent slight smallpox epidemic, I was shown a woman (Mrs. M. H—), aged 48 years, with an eruption of raised, irregularly shaped (apparently multilocular), œdematous papules or tubercles on red inflamed bases on the hands, forearms and upper front of the thorax. On September 26th these exudative spots were drying up, but there were one or two shotty papules about the wrists. On September 29th most of the spots had dried up and the eruption was disappearing. In this case I at first thought the eruption might be a very mild one of variola. But in addition there were some slightly purpuric erythematous lesions on the legs, and the history of the case was as follows: On September 22nd the patient had complained of the erythematous lesions and pains in the lower extremities and had been given a medicine containing pot. iodide, gr. v, three times daily. It

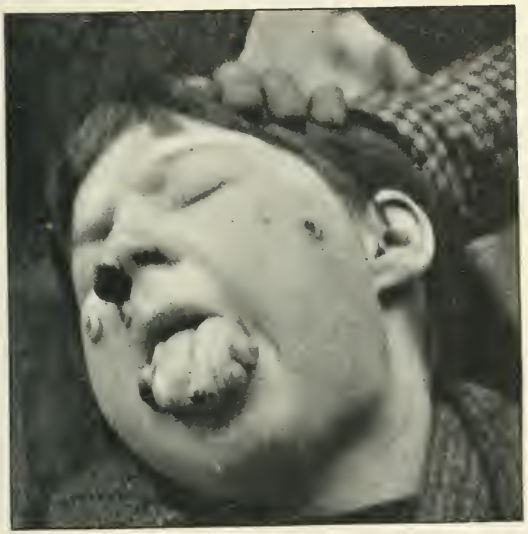

Fig. 4.—Granulomatous iododermia. Case 5.

was three days later when I first saw her with the above-described eruption on the upper extremities. The urine was free from albumin and sugar and the Wassermann reaction was negative. For an umbilicated, somewhat varioloid appearance of iodide lesions on the face of a cachectic man, aged 27 years, suffering from advanced tertiary syphilis of the pharynx, etc., see Tilbury Fox's case figured in the eleventh volume of the *Transactions of the Clinical Society of London* (1878, pl. iii, coloured).

Case 4.—A woman (K. S—), aged 36 years. The photograph (Fig. 3), for which I was indebted to the kindness of Dr. Block, shows a severe granulomatous iodide eruption, notably on the arms, from the use of potassium iodide in 15-gr. doses (April, 1902).

Case 5.—A girl (L. D—), aged 14 years, of whom I have the photograph reproduced here (Fig. 4), showing granulomatous nodules and swelling of the tongue and lesions of the face, apparently due to iodides. Together with the

tongue condition there was some salivation. There were also lesions on one leg. She had been taking syrup of iodide of iron, and then another doctor had given her 10-gr. doses of potassium iodide, three times daily, for a few days, on account of a suspicion of syphilis. In the hospital (August, 1902) there was bronchitis, with evidence of nephritis and pyrexia. The patient died, and the necropsy showed universal pericardial adhesion (not very old), much bronchitis and "large white kidneys." There was also ulceration of vocal cords. A history of former scarlet fever was obtained. I have to thank Dr. Leonard Williams for his kind permission to give this note of the case.

Here I would mention the severe "nodose" form of eruption by which bromism in infants often manifests itself, and this form may also be met with in breast-fed infants whose mothers are taking bromide. Thus in E. H. Molesworth's case* the baby was 10 months old, and had up to that time been entirely breast-fed and had been given no drugs, whereas the mother had for three or four months been taking nearly every night a sleeping-draught containing 30 gr. of potassium bromide. The lesions were on the child's forearms, hands and face; later on the trunk also, but to a lesser extent. They became crusted and granulomatous in appearance in eight to ten days from their commencement. In E. Graham Little's case† the patient was a breast-fed female infant, aged 9 months, and on one of

* Molesworth, "Case of Nodose Bromide Eruption in a Breast-fed Infant," *Brit. Journ. Derm. and Syph.*, 1917, xxix. p. 30.

† E. Graham Little, *Proc. Roy. Soc. Med., Derm. Sect.*, 1908, i, p. 73.

the legs the eruption consisted of very large "framboesioid" tumours, surrounded by a red areola. The child had not been given any bromide, but the mother, on account of epilepsy, was taking about 67½ gr. of potassium bromide daily. In five of F. C. Knowles's cases* of unusual type of bromide eruption in infants the bromide was transmitted through the mother's milk. See also F. van der Bogert on "Bromin Poisoning through the Mother's Milk"† and H. E. Smith's note on the same subject.‡ A. Whitfield,§ in his comments on Molesworth's communication, refers to similar cases of bromism through maternal milk recorded by Jonathan Hutchinson, jun.,‖ and Colcott Fox. The latter told me that in his case the mother was taking about 70 gr. of bromide per diem for epilepsy. J. Comby (1912) described such a case in an infant, aged 10 months.¶ A remarkable case of *congenital* bromodermia, observed in a boy a few days old, was described by J. Langer (*Jahrb. f. Kinderheilk*, Berlin, 1922, xcvi, p. 59). The infant's mother had been undergoing bromide treatment for epilepsy during her pregnancy.

(B) Facial, Pharyngeal and Intra-Oral Œdema, and Swelling of Salivary and Thyroid Glands in Cases of Idiosyncrasy towards Iodides.

Œdema of the loose subcutaneous tissue about the orbits is a fairly well-known symptom of iodism.** Probably feeble and cachectic persons are more liable to this than are others. Sometimes the whole face is affected, as it was in S. S. Lindsay's patient,†† an

* Knowles, abstract in *Brit. Journ. Child. Dis.*, London, 1909, vi, p. 80.

† F. van der Bogert, "Bromin Poisoning through Mother's Milk," *Amer. Journ. Dis. Child.*, Chicago, 1921, xxi, p. 167.

‡ H. E. Smith, "Bromism through Maternal Milk," *Lancet*, London, 1921, i, p. 825.

§ Whitfield, *Brit. Journ. Derm. and Syph.*, 1917, xxix, p. 33.

‖ Allbutt's *System of Medicine*, first edition, viii (1899), p. 926. The mother was under treatment for epilepsy.

¶ Comby, "Bromides cutanées chez les nourrissons." *Bull. de la Soc. de Péd. de Paris*, 1912, iv, p. 153.

** *Cf.* S. Ringer and H. Sainsbury, *Handbook to Therapeutics*, London, thirteenth edition, 1897, p. 140.

†† S. S. Lindsay, "Acute Œdema of the Face due to Potassium Iodide," *Lancet*, 1919, ii, p. 217.

arteriosclerotic man, aged 65 years, with a history of attacks of angina pectoris. In a case of œdema of the eyelids and face from potassium iodide that I observed in 1920 the patient (L. I—) was a "flabby" obese man, aged 45 years, with symptoms probably connected with hypopituitarism and a weakly positive Wassermann reaction. In another patient (R. M—), a man, aged 42 years, in whom I suspected pulmonary syphilis, I ordered 7½ gr. of potassium iodide three times daily (April, 1916). After four doses he developed conjunctival irritation and swelling not only of the face but of the fauces also, accompanied by a disagreeable taste in the mouth. It is also known (a very rare occurrence) that acute glottis œdema may arise as a result of iodide administered for syphilis or other reason, and that this may be accompanied by all the threatening signs of acute œdema of the larynx.

In a recent case (January, 1923) the acute œdema about the orbits and face was accompanied by sublingual œdema of the floor of the mouth. The patient (E. M—), a married woman, aged 43 years, was of delicate build, of the visceroptosis type (B. Stiller's "morbus asthenicus"), and there was some pyorrhœa alveolaris. Potassium iodide was given for bronchitic symptoms. After about three doses of 15 gr., each dose accompanied by ten drops of digalen, the iodide had to be discontinued, as the patient developed facial œdema, especially about the orbits, and œdema of the floor of the mouth below the tongue, together with an urticaria-like eruption on the trunk and head (very little on the extremities). She also complained of severe headache. A small subcutaneous injection of adrenalin chloride (Parke Davis & Co.) seemed to lessen these symptoms. The œdema of the floor of the mouth had practically disappeared by January 24th, and the facial œdema and urticaria-like eruption were almost gone by January 25th. From the history given by the patient it appeared that since 1914 she had been subject to occasional attacks of urticaria, sometimes with œdema about the orbits, and that she had also had swelling of the eyelids and face without any eruption on the trunk or extremities. She had, however, never previously had œdema of the mouth. It turned out also that on a previous occasion, when she was an in-patient, she had been found to have an idiosyncrasy towards potassium iodide. In connection with the facial and intra-oral œdema of January, 1923, it should be noted

that she had a menstrual period on January 22nd and 23rd, and this may possibly have increased her susceptibility to the iodide.

Swelling of the parotid or submaxillary salivary glands is recognised as an occasional manifestation of iodism. Possibly this is connected with excretion of iodide by these glands, for iodide, after being swallowed, quickly appears in the saliva, as it does in the urine, and increased excretion of saliva, with a metallic taste in the mouth, is a not uncommon result of taking potassium iodide. Leonard Williams* draws special attention to the involvement of the parotid glands: "A form of iodism which has often given rise to unfortunate mistakes is that which causes pain and swelling in the parotid gland, accompanied by other symptoms strongly suggesting mumps."

In the following case under my care in 1915 the submaxillary glands were involved. The patient (S. R—) was a weak-looking man, aged 34 years, with a slightly positive Wassermann reaction. After two 15-gr. doses of potassium iodide he developed headache, conjunctival irritation, coryza, a little pharyngeal pain on swallowing, and temporary decided bilateral swelling of the submaxillary salivary glands, especially the left one. This submaxillary swelling practically disappeared within three days, and so did the headache, conjunctival irritation and pharyngeal pain on swallowing. The patient probably likewise had quiescent pulmonary tuberculosis. I lost sight of him in 1920.

With the occasional swelling of salivary glands from iodism the cases of enlargement of the thyroid gland due to the same cause may be compared. In a hospital patient in 1901, a man (E. J—), aged 39 years, who had had primary and secondary syphilis seventeen years previously, whilst we were giving some potassium iodide and sodium salicylate for articular pains, we noticed a soft enlargement of the middle left portion of the thyroid gland, and there was considerable systolic pulsation in the neck. This was on February 4th, 1901. A peculiar staring appearance of the patient's eyes had been observed previously. When I saw him on March 7th the thyroidal enlargement and cervical pulsation were still present and there was tachycardia. I do not know the subsequent history of the case.

Various cases of acute thyroidal swelling and symptoms more or less resembling those of Graves's disease have been observed after and

* L. Williams, *Minor Maladies*, first edition, London, 1906 p. 282.

apparently excited by the use of iodides or iodine. A remarkable case of the kind following the application of iodine to an enlarged lymphatic gland behind the right ear was observed by Sidney Phillips* in 1901, and the discussion following the demonstration of the patient was most interesting.† On the Continent several records have been published of supposed acute non-suppurative toxic "thyroiditis" due to iodism‡; other cases of "Iodbasedow" (Kocher),§ or Graves's disease from iodide, have been described. In some but not all cases the patient had had syphilis. It may be here mentioned that pyrexia is a rare but acknowledged manifestation of both iodism and bromism, and that in one of A. Konried's two cases of "iodine-fever"‖ a so-called acute circumscribed "thyroiditis" was diagnosed. Acute non-suppurative "thyroiditis" of various kinds may be accompanied by fever.

A. Pasini has observed thyroidal enlargement from *bromism*, and thinks that the thyroid gland has a special affinity for bromine and iodine, as it normally contains those elements.¶

* S. Phillips, "A Case of Acute Bronchocele," *Trans. Clin. Soc. Lond.*, 1901, xxxiv, p. 236.

† Report in the *Lancet*, London, 1901. i, p. 626.

‡ J. Sellei, "Thyreoiditis acuta nach Gebrauch von Iodkali," *Arch. f. Derm. u. Syph.*, Vienna, 1902, lxii, p. 115; J. Sellei, *Deut. med. Woch.*, 1911, xxxvii, p. 549; M. P. Gundorow, "Zur Frage des Iodismus—Thyreoiditis jodica acuta," *Arch. f. Derm. u. Syph.*, 1905, lxxvii, p. 25; W. Lublinski, "Iodismus acutus und Thyreoiditis acuta," *Deut. med. Woch.*, 1906, xxxii, p. 304; W. Lublinski, "Thyreoiditis acuta," *Wien. med. Woch.*, 1910, lx, column 2498; W. Lublinski, "Die akute nicht eitrige Thyreoiditis," *Berl. klin. Woch.*, 1913, l, p. 834; F. Schütz, "Thyreoiditis jodica acuta," *Wien. med. Woch.*, 1908, lviii, column 1920.

§ Theodor Kocher, "Ueber Iodbasedow," *Centralb. f. Chir.*, Leipzig, 1910, xxxvii; *Beilage Verh. Deut. Gesellsch. f. Chir.*, p. 59; S. Goldflam, "Zur Frage des Iodbasedow," *Berl. klin. Woch.*, 1911, xlviii, p. 423; D. Picinew, *Russky Wratsch*, 1914, No. 7 (abstract in a German Journal); *cf.* also discussion reported in *Lancet*, London, 1901, i, p. 626.

‖ A. Konried, "Zwei Fälle von Iodfieber," *Med. Klinik*, 1911, vii, p. 998.

¶ A. Pasini, *Ann. de Derm. et de Syph.*, Paris, 1906, sér. 4, vii, p. 7. I have never myself noticed thyroidal enlargement from *bromism* and think that it must be very rare. Apart from severe bromodermia the most important harmful effects of bromide medication are probably the excessive somnolence and other cerebral symptoms occasionally observed, as a manifestation of idiosyncrasy, or in elderly and arteriosclerotic subjects. F. P. W.

NOTE.—As the abbreviation "gr." is frequently used on the Continent to signify grammes, I wish to state that in this paper it always signifies grains (15 grains to the gramme). F. P. W.

ARSENO-BENZOL IN THE TREATMENT OF SYPHILIS.*

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(*Continued from p.* 148.)

Other Methods of Administering the Arseno-benzols.

There is one method which I feel is perhaps worth recording, since I have not been able to find any mention of it elsewhere, which has surprised me, since one would expect it to be almost the first to be investigated.† In 1918 the writer tested the therapeutic value of "606" (kharsivan) when administered *by the mouth.* The acid aqueous solution was used in a dilution of 10 c.c. per decigram, since it was to come under the immediate influence of the hydrochloric acid of the stomach. After a few preliminary smaller doses which were tolerated without any symptoms, a course was scheduled consisting of four doses of 0.3 grm. in the first week on alternate days followed by one week's rest; the four doses were then repeated in the next week, making a total of 2·4 grm. "606" administered in three weeks.

Twelve cases were put on this course, which on paper looks somewhat alarming; however, none of them exhibited the slightest disturbance, gastric or otherwise. Clinically no appreciable influence could be demonstrated either with respect to disappearance of spirochætes from lesions,

* A paper read before the Congress of the Royal Institute of Public Health at Plymouth, May, 1922.

† Since writing this paper the author has found two publications in which are contained the following observations:

(*a*) ([21]) With the exception of a little vomiting and diarrhœa in some cases, salvarsan can be given by the mouth up to 0·6 gr. (? grm.) to human subjects without producing toxic symptoms. Thus administered, the drug exerts a therapeutic influence, but this influence is too feeble to warrant its use by this route.

(*b*) ([22]) Administered by the mouth arseno-benzol (salvarsan) is capable of producing a curative influence on the lesions of syphilis. The effect, however, is much less vigorous than when the drug is administered intravenously.

the healing of such lesions, or on the Wassermann reaction, which was tested weekly. Four cases developed fresh lesions in which spirochætes were found whilst under treatment in the third week. Finally one case received a total of 4·6 grm. kharsivan by the mouth in three weeks, and spirochætes were found after he had taken 3·4 grm. His Wassermann from ± at commencement became + + at the end of the third week. This patient developed slight albuminuria and nausea, both of which vanished with cessation of treatment. Such entirely unsatisfactory clinical findings rendered further investigation unjustifiable; after a week's rest, therefore, they continued with a course of kharsivan intravenously. They exhibited no intolerance during the latter, but one formed the impression that even after allowing for the three weeks which might be considered as three weeks wasted during the infection, they were exceptionally resistant to treatment. The proportion between the amount excreted in the urine to that in the fæces was not estimated in these cases. It has been stated that after an intravenous injection of "606" the bowels excrete from two to ten times as much arsenic as the kidneys (Fraenkel-Heiden and Navassart) ([23]).

Rectal Administration of the Arseno-benzols.

At one period the writer employed this method in the treatment of infants, and in conditions where one would hesitate to administer an intravenous injection, such as cases complicated by advanced or uncompensated cardiac conditions, aneurysm, renal insufficiency, etc. There were workers who advocated this route on the grounds that absorption taking place through the inferior mesenteric into the portal vein, there should be a greater likelihood of a large proportion of the dose being converted to the spirochæticidal derivative in its enforced passage through the liver.

However, I have abandoned this method long since, because even after taking elaborate care in the preparation of the patient and introducing the solution by very slow rectal infusion, absorption is too uncertain. One case in which I tested this method at Rochester Row, I found that three rectal infusions of "606," each containing 0·6 grm., given on successive days, entirely failed to produce any influence on the spirochætes in the surface lesions. One meets with no case, whatever the complications, in which it is impossible to administer arseno-benzol in the form

of the "914" deep subcutaneous injections, always provided that all due caution is taken as to dosage. In the writer's experience this is the safest means of resuming arseno-benzol treatment where indicated in a patient who has previously exhibited signs of intolerance.

On the Efficacy of the Arseno-Benzols in the Treatment of Syphilis.

How frequently each one of us here must have been asked, "Does '606' cure syphilis?"

It is impossible to attempt to answer this question unless we have some definite standard of postulates laid down that must be fulfilled in order that we can judge whether a case is cured or no. By cure do we mean that there is not a single spirochæte left in the patient? I can conceive of no possible alternative, and yet, not infrequently, one still meets with patients who have been told that they are probably cured and advised "to let the sleeping dog lie." In the light of our present knowledge, employing every available means, in what period of time are we justified in stating that every spirochæte has been destroyed and that none is resting like the sleeping dog, liable to wake up and "bite" after any local or general disturbance in the house? In the pre-salvarsan days frequently patients were pronounced cured on completion of two, three or four years' regular courses under mercurials and iodides, had they exhibited no clinical signs of a relapse during, say, the last year of treatment. At any rate, usually they were given permission to marry then should they wish. How frequently the subsequent Wassermann test now available has given a cruel disappointment even if such a case has been fortunate enough to escape a blatant clinical relapse! Of almost weekly occurrence do we meet with such cases showing a positive Wassermann. The cases of undoubted syphilis which were treated as above, which to-day give a permanent negative Wassermann, must be very rare indeed. Personally I cannot remember ever having met with one, where the original diagnosis was beyond suspicion, in which one could not provoke a positive Wassermann.

With the proofs constantly before us of the inadequacy of the older types of treatment which, in their turn, it was then considered resulted in cures, and the certain knowledge of the extraordinary length of time the spirochætes may remain quiescent, it is with exaggerated caution,

therefore, that we should draw up a standard of cure in order to estimate the capabilities of the arseno-benzols in this respect.

Should we be justified in stating that a case was cured, where, with the absence of clinical signs, the blood Wassermann remained negative over a period of five years after cessation of all treatment, the tests preferably being taken quarterly after a provocative injection of arseno-benzol, and the cerebrospinal fluid remaining non-pathological after such injection at yearly intervals, over the said five years? Up to the present, it has been extremely difficult in civilian clinics, or private practice, to collect more than a few isolated cases that have been subjected to the above rigid scrutiny. However, cases are turning up now in increasing numbers in which the five years since more or less systematic courses of arseno-benzol treatment terminated. No pains should be spared in thoroughly examining such cases when the opportunity is presented. Of recent years the average patient has taken a more intelligent interest in his treatment, and frequently is able to describe the preparation used, number and type of injections, and sometimes even dosage employed. Owing to the interruption in systematic courses of treatment in most of the civilian clinics during the war, for some time yet we must look to the Services, where circumstances and filed records have rendered it more possible, to provide us with increasing statistics of cases subjected to the more continuous observation over the full five years as advocated above.

Are we to accept the time-honoured belief that an uncured case of syphilis cannot contract the disease afresh, and *vice versâ*, that only a non-syphilitic can contract syphilis? If so, then an undoubted second infection of syphilis in a patient previously treated with arseno-benzol is an absolute proof that he was cured thereby. There are those who believe in the theory of "superimposed syphilis," *i. e.* that it is possible to superimpose a fresh syphilitic lesion on to an uncured latent syphilitic. Arguing along the lines of the "local resistance of tissue," one can conceive it possible to inoculate successfully a patient in whom, say, each secluded colony of spirochætes remaining from a previous infection is maintained in a forced state of quiescence by a surrounding zone of immune tissue of high resistance. Such may be the efficiency of each local barrier that a complete insulation is set up over varying periods of time during which the Wassermann will be negative. A sudden lowering of the local resistance of such a barrier, such as might result from trauma, would upset the balance, and what we recognise clinically as a "gumma"

would be the result. A lowering of the general resistance of the patient, such as that resulting from a prolonged drinking bout, or say an attack of influenza or malaria, might bring about a corresponding gradual retrograde-swing of the pendulum in the balance between the latent activity of the spirochætes and the resistance of each adjacent zone of immune tissue. The result would be a return of the Wassermann to positive, and were the balance further upset—possibly multiple gummata. One not infrequently meets with a case presenting a gumma of rapid development at the site of a preceding trauma, in which the blood Wassermann is still negative. If one were to test the blood of an old-standing tertiary syphilitic once a week for a year in the absence of all treatment, and the quantitative Wassermann results were indicated graphically on a chart, some very interesting " curves " would result. The most feasible explanation of the influence of a provocative injection of arseno-benzol upon the Wassermann reaction is in entire agreement with the preceding remarks. A case may be uncured, but with each residual focus of spirochætes held under such complete inhibition by the protective influence of local tissue resistance as to baffle detection if one were to rely merely upon a solitary Wassermann test. One cannot emphasise too strongly the importance of employing the provocative injection of arseno-benzol prior to ascertaining the Wassermann reaction both in the blood-serum and the cerebrospinal fluid when examining a patient with regard to cure. The interval of five days between the injection and the test is usually sufficient time to allow the tissues to have produced an increase in the Wassermann substance in response to the irritated spirochætes in sufficient quantity to be indicated in the test.

In old-standing cases presenting a definite lesion, in which the initial Wassermann test has given a weak positive reaction ($\pm$) which has been provoked to a single $+$, the writer has frequently noticed the reaction to increase to $++$ after the first three injections of arseno-benzol have been administered in the commencement of the course of treatment. It is a wise procedure, therefore, should a doubtful reaction be obtained after the provocative injection to repeat this injection a week later, and again read the Wassermann on the fifth day.

Some have criticised the " provoked Wassermann " adversely, even stating that a non-syphilitic's blood will give a positive reaction under the same conditions.

After a very considerable clinical experience with this method of

employing the Wassermann, having used it as a routine in every case attending for observation and for diagnosis (excepting early infections) for the past six years. I can only state that I am absolutely satisfied as to its extreme importance in rendering the "unprovoked" Wassermann more searching and therefore more reliable. In numerous instances has it yielded completely negative results. During the war, for instance, many patients suffering from various conditions were sent for investigation with the object of exclusion or otherwise of syphilis, so that one has had ample opportunity of applying it to non-syphilitics. In a limited number of cases the writer compared the results obtained on testing the blood on the second, third, fifth, seventh, fourteenth and twenty-first days following a provocative injection of arseno-benzol, and came to the conclusion that where a single injection only is employed, if there is no appreciable increased inhibition of hæmolysis on the fifth day, one is not likely to meet with it at the later dates. It is probable that in the near future more experimental work will be done, with a view to prove or disprove the possibility of superimposed infections of syphilis, but, unfortunately, unless one were able to carry out such investigation upon human beings it is difficult to see how reliable results could be obtained. It is for investigations such as this that the clinical potentialities of criminals and mentally deficients might be put to some service, possibly to lower the incidence of both in future generations by the advancement in treatment which would ensue from results so obtained.

If we feel disinclined to state dogmatically that the development of a second infection of syphilis is an absolute proof that the patient was cured of the first attack, yet I feel certain that all syphilologists will agree that one only meets with such second infections in cases in which the treatment of the initial attack has been extremely thorough. One might go further and say that it practically only occurs in those cases in which such treatment included thorough, intensive and prolonged courses of the arseno-benzols administered in the early stages of the first infection.

Of a certainty, if the original treatment had been scanty and interrupted, and not commenced until the infection was deep-seated, what subsequently might be diagnosed erroneously as a second infection is really a relapse. Such a mistake is of less importance to the patient, since he will be treated in either event, as compared with the misleading deductions likely to be accepted in discussing prognosis in general, and in

assessing the merits of various drugs and schemes of treatment. Such is the importance placed upon the occurrence of a second infection of syphilis by the vast majority of observant clinicians, in assessing the value of the treatment employed for the initial infection, that it may not be out of place to enumerate the postulates which the writer insists upon being fulfilled in order that he feels justified in diagnosing a second infection of syphilis in a patient.

(1) That there is absolute proof that the initial infection was syphilitic.

(2) That the treatment and the stage at which it was commenced were such as to justify a reasonable prospect of cure.

(3) That the Wassermann (preferably provoked) had been proved negative during the period intervening between the cessation of treatment and development of the initial lesion of the second infection.

(4) History of exposure and an incubation period compatible with a fresh infection.

(5) The sore must be situated on a site other than that occupied by the original chancre. This is very stringent, because it is liable to exclude possible genuine cases of second infection, since the contracted sclerosis left from the original chancre, such as at the frænum or the preputial orifice, is obviously a site most likely to provide an entry for the virus through a breach in the surface during coitus. However, it is better to err on the safe side of over-caution with the object of exclusion of the recurrent chancre.

(6) Clinically the sore, in which *Spirochæta pallida* should be abundant must present the features of an early syphilitic chancre as opposed to those of the types of recurrent chancre. If the sore has existed for as long as a week, there always will be palpable enlargement of the adjacent lymphatic vessels and glands into which it drains. The absence of the above is an important feature with a recurrent chancre.

(7) Thorough general examination fails to detect the presence of any co-existing recurrent syphilitic lesions.

(8) One would prefer to meet with the case sufficiently early that the Wassermann is negative, and remains so on the fifth day after the first injection of arseno-benzol, this being strong evidence in excluding both a relapse, and also a superimposed infection in an uncured case.

To those who are prepared to accept that a patient diagnosed under the above conditions as suffering from a second attack must have been absolutely cured from the original syphilitic infection, we can say definitely

that we do see such cases in which the arseno-benzols were responsible for the "cure" of the first infection.

The weak spot which strikes one at once in reviewing the literature containing descriptions and results of various schemes of arseno-benzol treatment, is the shortness of the subsequent periods of observation. The dates at which the spirochætes are unobtainable from accessible lesions, the rapidity with which such lesions resolve, and the behaviour of the Wassermann reaction in the blood and cerebrospinal fluid, are, of course, the routine data we have to rely upon in testing a scheme of treatment in the minimum of time.

What the profession and public want to know now, and in the future, on broad lines, is the subsequent progress and side-effects in a series large enough to be convincing, collected out of the enormous total of cases that has received thorough systematic courses of arseno-benzol treatment, throughout the civilised world, prior to the past five years.

There are available many cases in which the arseno-benzol treatment was commenced more than ten years ago that would provide valuable evidence if thoroughly examined to-day.

One hopes that in the future, from time to time, gradually increasing figures will be published as to progress as the all-important period under observation since cessation of arseno-benzol treatment lengthens out.

It should be the endeavour of every syphilologist to keep in touch with his patients as long as circumstances will permit. As the length of the period under observation increases, in direct proportion also does the value of the facts deduced; and our knowledge as to prognosis with regard to possibility of ultimate cure become based upon clinical facts.

Some Points in Favour of the Arseno-Benzols in the Treatment of Syphilis.

(1) At the time of writing, one feels safe in stating that in the arseno-benzol series we possess drugs capable of producing a maximum "smashing" effect upon the spirochætes with the minimum of danger to the host.

(2) The rapidity with which it is possible to render highly infectious surface lesions non-infectious in the out-patient is of great sociological importance.

(3) As a result of recent investigations, pain and inconvenience, which

were features of the earlier methods of administration, are being reduced to a minimum, as also are the immediate and remote toxic disturbances without lessening the therapeutic value of the products.

(4) Whilst under the arseno-benzol treatment it is being made more and more easy for the out-patient to continue his occupation in a state non-infectious to others.

(5) The above points considerably enhance the patient's likelihood of maintaining secret his infection; an important factor in lessening the incidence of concealment and resort to quacks.

(6) Up to the present date of observation one feels justified in stating that it is possible to cure syphilis with courses of arseno-benzols combined with mercury and iodides, always provided that treatment is commenced sufficiently early for the spirochætes to be accessible.

The type of case, therefore, with which one feels most confidence, is that in which treatment is commenced when the chancre is not yet indurated, the Wassermann negative, and remains negative on the fifth day after the first injection of arseno-benzol.

I have notes of four cases in my private practice who contracted a second infection of syphilis, one of which I have mentioned previously. In every instance the arseno-benzol treatment had been commenced immediately I had detected the spirochætes very early in the initial infection. In addition I have records of eleven patients, not including the five cases treated in 1911 with salvarsan intramuscularly already described, in all of whom the observation has now exceeded a period of five years, and the provoked Wassermann was negative when last examined in the present year. Seven were primary, and four were cases of secondary syphilis. None of the primary cases received less than 4 grm. of "606" intravenously, and 5·2 grm. was the minimum total administered to the secondary cases. In every instance the arseno-benzol treatment was supplemented with prolonged courses of mercury, alternating with iodides. Of course one has a larger number of cases at present under observation who bid fair to continue to give negative findings at the completion of the five years I have set up as some sort of standard of time. The writer is a firm believer in pushing the arseno-benzol treatment as intensively as the patient's tolerance will permit in small doses frequently throughout the first year, preferably by alternate intravenous and intra-muscular injections.

I am directly opposed to the procedure adopted by some workers,

namely, of withholding the arseno-benzols after the initial few injections, until the Wassermann reaction tends to become positive. My best results have always been obtained in cases in which the arseno-benzols have been persevered with in the face of a negative Wassermann throughout the first year of treatment, followed by smaller courses of arseno-benzol comprising three injections, given at each quarter in the second year, should the Wassermann still be negative and the patient tolerant.

The Limitations of the Arseno-Benzols in Syphilis.

The derivative which is formed in the tissues after the introduction of the arseno-benzols is capable of destroying the *S. pallida* provided it can reach them in sufficient strength; upon this all-important factor—the accessibility of the spirochætes—entirely depends the possibility of complete sterilisation, *i. e.* cure.

The chance of sterilising the patient of spirochætes becomes increasingly difficult in proportion to the time allowed to elapse after infection before treatment is commenced, the reason for this being that the spirochætes have had time after the initial septicæmia to reach recesses sheltered from the blood-stream. It is due to the power which *S. pallida* possess of remaining latent in such avascular retreats for years that syphilis has well deserved the intractable reputation it possesses. No matter what drugs may supersede the arseno-benzols in the future, they will be faced with the same problem of penetration. There is an open field for serum and vaccine therapy in syphilis, and one feels it is possible when methods have been devised to facilitate the culture of the spirochæte, that from this direction the next important advance may accrue.

An important point upon which I think most clinicians will agree, is the variation with which individual cases, presenting a clinical similarity with regard to duration of infection, respond to a uniform course of arseno-benzol treatment.

My own view is that the therapeutic value is largely influenced by the rate of excretion. A patient who eliminates a given dosage slowly does better clinically with regard to his syphilis than a patient who excretes the same rapidly, but is a likely candidate to develop side-effects, such as dermatitis and jaundice. The slower the excretion the greater the chance of a larger proportion of the injected dose being converted into the spirochæticidal derivative. As previously enlarged upon, this is very notice-

able in the "914" series, in some preparations of which excretion is very rapid after an intravenous injection, much coming through the kidneys probably unchanged.

In comparison with a deep subcutaneous injection of the same preparation, where excretion is slower, there is an increased therapeutic value dose for dose, because there is a greater production of the active derivative.

The type of case in which the arseno-benzols seem unable to effect a cure—although their careful employment may ensure a ripe old age to the patient—is the case carrying an old-standing infection possessing multiple impermeable sclerosis harbouring spirochætes.

(I have demonstrated *S. pallida* in the dense sclerosis of a chancre, excised and sectionised twenty-four years after infection.)

Involvement of that avascular structure—the *cornea*—is, in my experience, unaffected by the arseno-benzols when administered subcutaneously or intravenously. (The beneficial effect of the subconjunctival injections is mentioned elsewhere.)

Gross involvement of the *parenchyma* of the central nervous system, as in general paralysis of the insane, is, as yet, disappointing in the great majority of cases under arseno-benzol medication.

In recesses harbouring spirochætes in the general tissues—no matter how the drug be administered—we have to rely entirely on the possibility of its derivative gaining access to the spirochætes by means of the blood-vessels which, unfortunately, in and around such foci undergo gross pathological derangement, resulting in a breaking down of transport where most desired.

The arseno-benzols can be *tolerated* only in carefully graduated doses separated by intervals of rest to allow for excretion in order to avoid the danger of toxic damage from accumulation. The "rest" intervals are also imperative to allow the essential structures of important viscera to recuperate from the irritation, if not actual damage caused by the toxic effect of the arseno-benzols. The endothelium of the end-vessels of all the excretory organs is particularly liable to damage. Therefore one cannot keep a patient for an indefinite period constantly under the arseno-benzols. One feels that, owing to this fact, mercurial treatment is such a valuable adjunct to tide over these forced intervals of rest. The iodides are also indispensable on account of their power to promote absorption of partially organised infiltrates, and in opening up the lumen of vessels

already constricted or even occluded by syphilitic endarteritis. Thereby they assist in the penetration of the arseno-benzol derivative, together with the antibodies in circulation. It is claimed also that the elimination of the arseno-benzols is facilitated by the iodides, as in the case with mercurials.

Dangerous Relapses.

There is a very important point I should like to emphasise with regard to the arseno-benzols in the treatment of syphilis, and this is the dangerous nature of the relapses one meets with in those cases insufficiently treated. These relapses are dangerous—not only from the patient's point of view, but sociologically, on account of the highly infectious nature of the surface lesions prone to develop at a date considerably later than is one's experience with similar relapses in cases treated purely with mercury—or, in fact, in which no treatment at all had been received. The writer has seen such lesions as moist papules, mucous patches and condylomata develop as relapses in patients as late as six years from commencement of arseno-benzol treatment in primary and secondary cases.

The exudate from such lesions being rich in spirochætes, one will at once realise the certain disasters that are bound to occur should such a patient have been given permission to marry, say, in the fourth or fifth year.

The possibility of the occurrence of such delayed highly infectious clinical relapses serves only to emphasise the importance of keeping patients under regular and prolonged observation where the arseno-benzols are employed in the treatment of syphilis. Why should cases insufficiently treated with the arseno-benzols be prone to relapse in the stage at which treatment was commenced—say even six years previously—as compared with the practically non-infectious gummatous lesions one would meet with at this date in cases treated solely by mercury, or had received no treatment at all ? The explanation must rest in the production of antibodies. In the absence of treatment, or in the case treated solely by mercury, there is no sudden destruction of practically every spirochæte that can be reached through the blood-stream, as with the early injections of the arseno-benzols.

The patient, therefore, has to deal with the spirochætal septicæmia, as with other infections, by the production of specific antibodies.

Unfortunately the protection thus provided is always inadequate,

but in varying degree, with the result that we witness the gradual evolution of the infection as it passes through the time-honoured phases recognised as the clinical milestones—the primary, secondary, and tertiary periods. However, from a sociological point of view, Nature has not been so indolent as this might appear, since she does not leave the unfortunate patient in a state capable of transmitting the infection to others for the remainder of his existence. It was Fournier who first emphasised the four years' "danger period" at the termination of which it was safe for a male patient to marry. One sees numerous practically untreated cases in which marriage has taken place at a date beyond the four years, although the husband may be exhibiting a definite gummatous lesion, in which the wife and subsequent children escape infection.

As we have just stated, this natural and certain evolution in the disease is very considerably modified under the employment of the arseno-benzol therapy. The sudden massive destruction of the accessible spirochætes "stops the clock," as Colonel Harrison has aptly described it, in the natural production of antibodies.

Such residual spirochætes as have escaped the barrage will shelter quietly in their "dug-outs," apparently producing no more local or general disturbance than during the period of incubation following the initial inoculation.

When, however, they proliferate and again emerge into the open field they meet with practically virgin soil, no more protected than it was against the initial campaign.

One not infrequently sees a number of surface lesions in a case relapsing after arseno-benzol treatment, which very closely resemble the primary chancre. Again, in other cases, probably the most frequent, one sees the first recurrence in the site of the original chancre, *i. e.* the oldest and therefore the most protected recess. If treatment has not been commenced the relapsing chancre will be followed by a spirochætal septicæmia, and the usual accompanying skin and mucous membrane lesions will subsequently appear—in fact, he is in the ordinary secondary stage of the untreated syphilitic.

The neuro-recurrences which most clinicians agreed were met with far more frequently after the introduction of the arseno-benzol therapy in syphilis can be similarly explained by the insufficient application of the remedies failing to sterilise the meninges and vessel walls of residual nests of spirochætes. With the advances which have been made in recent

years—both in the administration and the total amount of arseno-benzol given in courses of treatment—neuro-recurrences are much less frequently seen to-day. Fortunately, if recognised before irreparable damage has ensued, the condition responds rapidly to treatment when resumed.

The fact that all clinical relapses respond rapidly to the resumption of arseno-benzol treatment is strong evidence against the theory of the production of the "arsenic-fast" strain of spirochæte.

Toxic effects.—With regard to the toxic effects of the arseno-benzols, the writer feels confident that with the new light which is being thrown on the hitherto obscure ætiology, both from clinical and pathological researches, the future will show a progressive diminution in the incidence of side-effects, which are still the dread of every clinician. There would seem to be a parallelism between the rate of excretion and the development of symptoms of intolerance.

Take for instance exfoliative dermatitis. If we carefully question the patient in whom this condition has developed, we can elicit almost invariably symptoms of intolerance, such as we recognise clinically, to have followed the injection or injections which preceded the last prior to the "flare-up": symptoms such as enervation, loss of sleep and appetite, chronic headache, especially when described as a "bursting" or feeling of weight behind the eyes. With these there may be occasional vomiting or feeling of nausea, diarrhœa, pain in the loins, and deep muscular tenderness and cramp. Each, or a group of these symptoms, may not appear until twelve or more hours after an injection, and unless as a result of careful inquiry on the part of the surgeon, in all probability will not be mentioned by the out-patient at his next attendance for another injection. I feel sure that in the majority of cases developing vague symptoms as just described, were they tested as to the rate of excretion of the drug it would be found to be delayed. Now that we are familiar with the importance of such symptoms, as also with certain of the more immediate side-effects, injections are being withheld, which in the past might have been administered. Such an injection if given is exceedingly likely to be "the last straw" to the already damaged structures. With the accumulation of clinical experience with regard to size and spacing of dosage, together with a more accurate recognition of the earliest warnings of intolerance, *dermatitis*, *jaundice* and *cerebral symptoms* should become of increasingly rare occurrence.

There are, moreover, certain types of patients now recognised as being likely candidates to develop *dermatitis*, for instance, whilst under the arseno-benzols. It is possible that the endothelium of their end-vessels is being irritated already by a toxin other than that of syphilis, and so less likely to withstand the additional irritation of the arseno-benzols. The recent view advanced by dermatologists is that the respiratory and alimentary tracts frequently provide the sources from which the toxin is derived in the ætiology of certain chronic dermatoses. Patients suffering from pre-existing chronic dermatoses are very prone to develop exfoliative dermatitis under the arseno-benzols.

The diabetic, alcoholic, and subject of chronic Bright's disease, whose end-vessels are in a state of chronic irritation, should be treated with extreme caution. Again, the patient whose organs of excretion, either skin, kidneys, liver, or intestines are deranged, calls for very careful observation and modification in arseno-benzol treatment. Diminished function in any one of these throws additional stress on the others.

Jaundice.—At the present day, when so large a total of patients is undergoing arseno-benzol treatment, to which must be added those who have received the same in the recent past, we must not lose sight of the fact that we are always faced with a definite incidence of jaundice, from whatever cause, in a corresponding total of the population never having received arseno-benzol.

Firstly, one would like to have accurate figures of the yearly incidence of jaundice in the general population, and secondly, what increase there is amongst those who have received arseno-benzol treatment.

There are those whose liver-cells and ducts are already being irritated by an agent other than arseno-benzol, which may then "fire the spark."

Further, one would like some weight of evidence derived from the microscopical examination of the livers of patients previously treated with arseno-benzol who have died from some extraneous cause during, and at various intervals after, such treatment.

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REPORT OF A FATAL CASE OF DERMATITIS FOLLOWING ON THE ADMINISTRATION OF A SINGLE DOSE OF NOVARSENOBILLON.

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Much has been written concerning the toxic manifestations of arsenobenzene and its derivatives and the types of dermatitis and toxic erythemata which may follow their administration. At the present time there is still much conflict of opinion regarding the ætiology of such toxæmias as hepatitis and nephritis, and it is not clear whether the disease which is being treated, the therapy as a whole, the arsenobenzene in particular, or a combination of all three is the responsible and determining factor. In the case of toxic erythemata, however, opinion appears agreed that the determining factor undoubtedly is the arsenobenzene itself together with such accessory factors as specialised or generalised individual idiosyncrasy. The bulk of the evidence, also, appears to throw the responsibility on the arsenical rather than the amino radicle in the preparation employed. Much also has been written belittling the serious responsibilities which are inseparable from the administration of arsenobenzene in large intravenous doses. One is entitled to suppose that, where points of view are so diametrically opposite, the former would have some modifying influence on the latter. As far as one can judge, however, no such fortunate result has occurred. Indeed it would appear that the writers from the first viewpoint regard the others with scepticism and probably find them guilty of just a little mild exaggeration, while they in turn consider the latter as near-visioned or at least exceedingly fortunate in their therapeutic experiences.

I have endeavoured to show elsewhere ([1, 2]) that small-dose arsenobenzene therapy in syphilis is superior to the more generally accepted massive-dose procedure, that therapy should not be scaled to any mechanical time table, that the Wassermann reaction as a control of treatment is utterly fallacious, and that one is much more likely to attain one's immunising objective by slow and gradual increase of the immunity

curve than by any rapid and dramatic sterilisation of the systemic circulation. While all of these considerations have a direct bearing on the incidence of arsenobenzene toxæmias, it is the last named which particularly concerns us in a consideration of such catastrophies as that illustrated by the case under review.

Rapid sterilisation demands the unrelenting administration of massive intravenous doses of arsenobenzene or its derivatives to the utmost point of human tolerance. The only safety valve in such a procedure is the fact that those who practise it rely on the Wassermann reaction as a control. As a result of rapid partial sterilisation the Wassermann reaction becomes negative very quickly, treatment is discontinued, and the point of tolerance is not over-reached. This is interpreted as satisfactory from the point of cure. In point of fact it is only satisfactory in that it calls for discontinuance of heroic treatment and the patient's tolerance is left intact, even if "cure" be further off than ever. In a certain small percentage of cases the patient's powers of dealing with arsenobenzene are exceedingly high, and his Wassermann reaction remains positive. Large doses are continued for a time, but, since rapid sterilisation as understood by this school has not been attained, treatment is again discontinued, and the case is classed with those few exceedingly fortunate individuals as "Wassermann-fast." In point of fact the large dose to such an individual is precisely what the small dose is to the normal healthy adult. The process which has been under way has been one of slow sterilisation, and, as is usual with cases treated by small doses over long periods, the Wassermann reaction would have become negative in nine, twelve, or twenty-four months' time. The point which emerges, therefore, is that it is fortunate that the tolerance of the so-called "Wassermann-fast" patient to arsenobenzene is high.

Now it follows that whatever may be the worker's views regarding the respective merits of large- or small-dose therapy in syphilis (that is to say, rapid or slow sterilisation), it is essential for the safety and well-being of the patient to estimate, however roughly, what his tolerance to arsenobenzene is likely to be. Debon has demonstrated his method of estimating the rate of arsenic elimination. By charting out this rate, and administering successive doses only after the previous dose has been completely eliminated, he considers that the safety of the patient is guaranteed. It is difficult for all of us to have quantitative estimations of eliminated arsenic carried out, but it is not difficult to commence

treatment with infinitesimal doses and watch the clinical behaviour of the patient.

It may be argued that the reason for employing massive doses from the beginning is one of urgency, and that this cannot be met by the employment of small doses, which would involve the loss of time when it is most valuable. Further, the objection has been brought forward that as a result of continued small doses the spironemata become arsenic-fast, and that one therefore defeats one's own end in this way. When it is pointed out that the principle involved in treatment by continuous small doses depends on the faculty arsenobenzene possesses to stimulate antibody-production and not on any parasiticidal properties, and that the body immunising mechanism is capable of dealing with spironemata, whether they be arsenic-fast or not, the latter objection is disposed of. That the former argument is without foundation has been proved by the clinical experience of those who have employed continuous minute intravenous or subcutaneous doses over long periods even in the earliest stages of the disease. It may be of interest to those who attach importance to the phenomenon that in cases of early syphilis so treated, the Wassermann reaction, which becomes negative slowly and insidiously, often after many months of gradual and imperceptible immunisation, remains negative indefinitely.

It has been stated by McDonagh that "if intramine (diortho-diaminothio-benzene) were only universally employed in conjunction with arsenobenzene, not only would cases of arsenical dermatitis be never seen, but all the other toxic manifestations would become rarities." When one considers that the protection which the systematic employment of intramine gives to the patient receiving massive-dose therapy is considerable, one may state that the safety it affords when employed conjunctly with small-dose therapy is well-nigh absolute. If 0·15 grm. is looked upon as the maximum intravenous dose of novarsenobenzene, if intramine—or, according to McDonagh's latest pronouncement, contramine—is included in the treatment routine, and if danger-signals are accurately assessed, accidents will not occur either early or late during the course of anti-syphilitic treatment. So long as arsenobenzene therapy remains the high-water mark of efficiency in the treatment of early syphilis; so long as the risks of accident or catastrophe at present inseparable from the use of arsenobenzene remain; and so long as intramine is unsurpassed as a therapeutic agent of its class, whatever be its mode of action, so long

are we unjustified in excluding it from any *course* of treatment which entails the administration of arsenobenzene, whether the doses employed be massive or minute.

Arsenical dermatitis may follow the first dose of arsenobenzene, or it may occur as long as eighteen months after treatment has been suspended (McDonagh). I have seen on several occasions a severe exfoliative dermatitis follow a single dose of 0·3 grm. of galyl, kharsivan, neokharsivan and novarsenobillon. I have never seen a severe accident follow an initial dose of 0·05 or 0·15 grm. of any novarsenobenzene preparation. Rigor, fever, diarrhœa and albuminuria and less frequently transient dermatoses have been met with following the first and several subsequent 0·075 grm. doses. It is reasonable to suppose that in these cases, had the initial dose been larger, more serious accidents would have resulted.

The great variety of eruptions which may follow the prolonged small-dose administration of arsenic was appreciated long before the advent of arsenobenzene. The same variety is recognised when associated with arsenobenzene whatever be the respective parts played by the arsenic and amino-benzene radicles. Starting as an eruption of small vesicles usually upon the forearms and face, as a scarlatiniform erythema, or it may be as a formication and pruritus in the arches of the feet or backs of the hands, it may rapidly develop into a true *dermatitis exfoliativa* varying in type and intensity from a *pityriasis rubra pilaris* to a *pityriasis rubra seborrhoica*, or, where patchy, may closely resemble the pre-mycotic condition of *mycosis fungoides* (to borrow McDonagh's excellent simile), going through the same urticarial, erythematous, vesicular or eczematous evolution. When fully developed the condition is always a serious one, and the patient's life should be considered in danger whether the toxæmia follows an initial injection of arsenobenzene or a series of injections.

The reason for reporting the following case turns on the fact that a fatal termination following a single administration of arsenobenzene is an occurrence of extreme rarity.

Report of Case.

Patient.—The patient was a coloured man belonging to one of the numerous half-breed bastard races so characteristic of the indigenous population of the Cape Peninsula. His age was 39 years, and, as a typical brand of the heterogeneous stock from which he sprang, he was

small, lean, ill-equipped with muscle, brawn, brain or intelligence—altogether a miserable specimen of even his own low type of the human species. He spoke English badly, a fact which made interrogation, history-taking and nursing difficult. His habits were dirty and reprehensible and he was apparently accustomed to filth and squalor. If a number of flies alighted on his eyes or nose, he did not trouble to brush them off, but simply allowed them to crawl maggot-like over his face. He smoked interminable cigarettes, took his food as a matter of course, and evinced no material interest in his malady, his treatment, his companions or his surroundings. Life to him, one gathered, was merely the proposition of existence, and he contributed little or nothing to the struggle.

History.—Some three months previously he had presented himself at the Out-Patient Department of the New Somerset Hospital, Cape Town, complaining of hoarseness, sore throat and difficulty in swallowing. His serum Wassermann reaction proving positive, he was referred to the out-patient Venereal Clinic for treatment. There he received but one injection, which, on inquiry at the Clinic, proved to be 0·30 grm. novarsenobillon. Two days later two small blisters roughly about the size of a pea appeared on the arm near the site of the injection—quite a usual site for the appearance of a transient erythema. At first he took no notice, but four days later he discovered numerous crops of similar vesicles over his thorax, abdomen and groins. He did not recollect particular implication of the face. These vesicles or bullæ varied in size from a pea to a florin. They rapidly dried up, leaving crusts which came off here and there, small red areas corresponding in size to that of the vesicle remaining. A week later he reported his condition at the Clinic, and was sent home to bed. There he remained, his condition becoming steadily worse, until the time of his admission to hospital, when he came under my care.

His account of the date and manner of his syphilitic infection was vague and contradictory. He remembered a sore on his penis some twenty years previously, but this healed without sequela. His present chancre appeared to have occurred just about two months before he received the injection of novarsenobillon. He had no definite ideas when his syphiloderm and sore throat made their appearance, but one gathered that they were quite recent when he presented himself for treatment in the first place. The conclusion, therefore, was that his syphilis was of five months' duration, and that he had spent three months in bed at his home suffering from an untreated arsenobenzene dermatitis.

Condition on admission to hospital.—When I first saw the patient he was clearly seriously ill. His temperature was normal and his pulse-rate 64 per minute. He ate well and slept badly, and his bowels moved naturally twice daily. There was some congestion of the bases of both lungs and corresponding impairment of note, but nothing more. He had no cough or other bronchitic symptoms.

The rash.—On the few small areas of skin surface not implicated in the arsenobenzene eruption extensive dark luetic pigmentation could be seen standing out on his dusky skin. The rash, however, covered practically the whole skin surface from head to foot. It varied much in character and orientation in different situations, and is therefore somewhat difficult to describe. Perhaps this can be done most lucidly by drawing comparisons with skin conditions whose clinical appearances are well known. The face and neck escaped more lightly than the skin elsewhere, except for the margins of the ears, eyes, nose and mouth. There the picture closely resembled an *erythema iris*, producing raised purple spots, here and there covered with exudate. The ear margins were excoriated and ulcerated, and oozed a profuse sanguineous serous exudate which dried and crusted. In the same way the eyelids, nostrils and lips were affected, and the profuse exudate trickled over his face until it dried. The condition spread to the buccal mucous membrane, where it was converted into definite small ulcers which bled readily and often.

The arms, hands, legs and feet showed a condition closely resembling a severe form of *erythema multiforme*. It was most severe on the hands, elbows and ankles. The production of low-lying bullæ was extensive and superficial hæmorrhages were numerous. There was much secondary infection and superficial sepsis. The trunk and thighs, both back and front, were implicated in a destructive hæmorrhagic eruption of the *pemphigus foliaceus* type on a large scale. The bullæ varied in size from a florin to something much bigger than the palm of one's hand. These were never tense, but burst and frizzled up very quickly, curling to the edges of vast denudated hæmorrhagic areas like crinkling flakes or withered leaves. The sanguineous exudation was profuse and evil-smelling, and everywhere tended to dry up in a sticky gelatinous serpiginous mass. The chest, abdomen, back, buttocks, perineum, scrotum and penis were all similarly involved to an extent which, were it adequately described, would leave an impression of unmitigated exaggeration. The stench which emanated from the patient and his bed clothing was incapable of description.

The mouth.—Stokes (3) has drawn attention to the fact that foci of septic infection increase the susceptibility of the skin to arsenical damage. In this case the mouth was in a shocking condition, and although its state was not observed before the dermatitis occurred, it is highly probable that there was an extensive dental and oral sepsis present. There was some leucoplakia on the back of the tongue. The tongue was heavily coated and very much swollen, and its edges were ulcerated and bleeding. There was much stomatitis and gingivitis, the ulceration of the lips and buccal surfaces extensive, and the hæmorrhagic ooze almost continuous. The breath was foul and foetid. In spite of this condition he ate his food well, and on occasion voraciously, and smoked numerous cigarettes. The latter were the only thing he asked for and seemed to afford him much pleasure and relish. Since a fatal termination was inevitable, these were not denied him.

The eyes.—In addition to the extensive ulceration of the eyelids with its profuse exudation and encrusted edges, there was a severe bilateral conjunctivitis together with numerous small subconjunctival hæmorrhages. The lids were constantly glued together in spite of constant bathing. Vision was unimpaired, and, curiously enough, there was no photophobia.

The central nervous system.—No changes were made out except that the Achilles jerk was absent on both sides.

The urine.—The daily output of urine varied from 40 to 50 ounces. Its specific gravity was high (1030), and it was acid in reaction. There was no albumen, sugar or bile. Examination of the centrifugalised deposit showed the presence of a few degenerate cells and urate crystals.

The blood.—The serum Wassermann reaction was strongly positive. Erythrocytes showed some slight alteration in size and staining. There was no obvious leucocytosis. The differential count was made up as follows :

Polymorphonuclear leucocytes . . .	66 per cent.
Lymphocytes (large and small) . . .	28·5 ,,
Large mononuclear leucocytes . . .	2·5 ,,
Eosinophiles	3·0 ,,

To all intents and purposes, therefore, the blood picture was normal.

General condition.—The patient was desperately ill. He appeared quite satisfied with his condition, but remarkably disinterested. There was no marked emaciation or cachexia. He suffered no pain, and was extraordinarily stoical regarding irritation and itching. The fœtor was

appalling in spite of every effort to control it. In spite of the vast areas of superficial sepsis he did not appear toxic, and the absence of any evidence of septic absorption was particularly surprising. The pulse-rate varied very little, its limits being 64 to 68 per minute. The temperature was never raised. Respiration was never interfered with, and there was a complete absence of bronchitic or pneumonic symptoms. Adenopathy was general and advanced. Liver dulness was diminished. There was no icterus. The spleen was not enlarged sufficiently to be palpable. Only the scalp and nails escaped the general involvement of the widespread destructive eruption.

Treatment.—The patient was immediately moved to an open verandah, where he had the benefit of fresh air and sunshine, and where, by the mitigation of the fœtor, his neighbourhood was tolerable. Bed clothing was plentiful and every precaution was taken against chilling—an exceedingly important point in the management of these cases. Food was light and the fluid intake considerable. The patient was bathed from head to foot twice daily, and the extensive implicated surfaces were dressed with calamine cream and swathed in gauze. For the rest, intramine was relied on, although it was realised that much could not be expected of it, for its employment was much too long delayed. However, 3·0 c.c. was administered intramuscularly every fourth day, without pain and without reaction. In all five doses were given (15 c.c.), but no improvement was noted.

Termination.—The case terminated fatally 22 days after admission to hospital, and 112 days after the first appearance of toxic symptoms.

Post-mortem report.—Prof. G. B. Bartlett, University of Cape Town, reported that the appearances of the organs were typical of the series of cases of salvarsan poisoning examined by the London Hospital Pathological Institute for the Medical Research Committee.(4)

I am indebted to my house-surgeon, Dr. H. Hodgson, for extracting a coherent history in this case under peculiarly difficult circumstances.

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(2) *Idem.*, and Duncan, A. G. B.—*Brit. Journ. of Derm. and Syph.*, 1921, xxxiii, Nos. 7 and 8, pp. 251, 281.

(3) Stokes, J. H.—*Med. Clin. N. Amer.*, 1919, iii, p. 844.

(4) Special Report Series, Medical Research Council, London, No. 55, 1920.

CURRENT LITERATURE.

INFLAMMATIONS, ETC.

A CASE OF ACANTHOSIS NIGRICANS. L. Brunetti, E. Freund and A. Sturli. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1921, fasc. vi, p. 695.)

The authors report a typical case of acanthosis nigricans, with very good photographs of the eruption and section of the skin. They also give a short *résumé* of all the other fifty-three cases hitherto published. The case was a girl, aged 18 years, who, though fairly well developed, showed signs of infantilism with poorly developed genital organs. Patient had not menstruated. Thyroid gland was scarcely palpable. Radiographs showed that the sella turcica was smaller than normal. The authors suggest that the patient was the subject of diminished function of the endocrine glands, and the treatment was based on that hypothesis. She was given ovarian extract and X-rays in large doses applied locally to the skin lesions; this caused marked improvement, the papillomatous areas flattening down and the pigmentation disappearing. The skin showed marked toleration of large doses of X-rays. X-rays were later applied to the thyroid, ovaries, pituitary gland and the area of the thymus gland. This treatment had no effect on the amenorrhœa or on the signs of infantilism, but the patient's growth seemed to be accelerated. She gained 10 kgrm. in weight in a few months. The authors draw no definite conclusions from this case. They think that the condition of the endocrine glands should be considered in all cases of acanthosis nigricans, and that in cases where carcinomata occur there may be some dystrophy and new-formation in the various organs, and these individuals may have a diminished function of the endocrine glands and a lessened constitutional resistance. R. C. L.

ON GRANULOMATOUS (NODULO-GUMMATOUS) FORMATIONS FROM THE COMMON PYOGENIC ORGANISMS. R. Porcelli. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. i, p. 23.)

The case was a woman, aged 55 years, who showed a large furunculoid lesion on left ala nasi. This lesion ulcerated deeply and perforated the ala nasi. A similar lesion then developed above the zygoma on right side and also ulcerated deeply. Clinically the lesions looked not unlike ulcerating gummata or carcinomata. Microscopically the epithelium over the edge of the lesion showed considerable acanthosis with prolongation of the interpapillary projections. The corium showed a large granulomatous mass with epithelioid and giant-cells. In places the giant-cells could be seen developing from the endothelium of capillaries. There were also a large number of polymorphonuclear leucocytes and lymphocytes. From the lesion a pure culture of *Staphylococcus pyogenes albus* was obtained. This gave a positive agglutination test with the patient's serum in a dilution of 1 in 360. An emulsion of this organism injected subcutaneously in the deltoid region produced after 6–8 days an indurated lesion which slowly increased in size till the 14th day, when it became softer and rapidly retrogressed. Injected subcutaneously in a rat, it produced a similar lesion,

which slowly disappeared without ulceration in thirty-six days, and microscopic examinations of this lesion showed numerous cocci in the central area. Microscopically it showed a granuloma with polymorphs, lymphocytes, and a few giant-cells. Similar lesions, spontaneously healing, were also produced in guinea-pigs, and from these the organism was recovered. The author, therefore, concludes that the common pyogenic organisms may, if specially attenuated and the individual be susceptible, produce true granulomatous swellings similar to those seen in tubercle, syphilis, fungus diseases, etc. R. C. L.

CONTRIBUTION TO THE STUDY OF THE ÆTIOLOGY OF "HERPES SIMPLEX." A. Fontana. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 96.)

The author succeeded in inoculating the virus obtained from the vesicles of herpes labialis on the skin of the forearm of other patients, obtaining typical vesicles after an incubation period of forty-eight hours. He also inoculated the virus on to the cornea of the rabbit, producing a keratitis, from which he succeeded in re-inoculating the forearm of a human being, producing vesicular lesions. From these skin lesions a rabbit's eye was again infected, and from the eye the skin of a human being was again inoculated so as to produce typical lesions. The inoculations were made by transferring serous fluid from the vesicular lesions. No organism is described. R. C. L.

AN EPIDEMIC OF "PEMPHIGUS EPIDEMICUS." M. Trossarello. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 98.)

A bullous eruption affecting children and adults, but chiefly the former, was seen in August, 1921, in several towns on the coast of Italy. It seemed to affect those who attended the baths. The general health was good. The lesions consisted of bullæ of various sizes arising on normal or slightly reddened skin. At first the blebs were filled with clear fluid, which later became sero-purulent, the bleb bursting and forming a crust. Each lesion took from four to six days to run its course. The regions affected chiefly were the limbs, nates, trunk and face. The palms and soles were never affected. In one case a whole family, both parents and children, were attacked. The author thinks the cases corresponded to epidemic pemphigus or pemphigus neonatorum. From the blisters a diplococcus was obtained corresponding to the *Diplococcus non-capsulatus* recorded by Pasini. This epidemic was peculiar on account of the number of adults attacked and the benign nature of the disease. The author thinks the infection was conveyed chiefly by towels at the baths. R. C. L.

A CASE OF CIRCUMSCRIBED ANGIOECTASIC ERYTHRODERMIA OF THE LIMBS AND FACE, PROBABLY OF ENDOCRINE ORIGIN. D. Majocchi. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 134.)

The case described was a girl of 17, who showed on the lower part of face and lower limbs red, reddish-brown or reddish-blue areas which showed very marked dilatation of the skin capillaries. The skin of the areas, especially on the legs, was scaly in some places. Her blood-pressure was 210–220 mm. The author considered the condition as probably of endocrine origin. Local astringent applications, together with the administration of thyroid, caused a considerable

diminution in the dilatation of the vessels during the six months that the patient was in hospital. R. C. L.

DERMATITIS CHRONICA ATROPHICANS OF PROBABLE TUBERCULOUS ORIGIN: A CLINICAL, HISTOPATHOLOGICAL AND EXPERIMENTAL STUDY OF THE SO-CALLED IDIOPATHIC ATROPHY OF THE SKIN. C. Ducrey. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 596.)

This is the first case of idiopathic atrophy of the skin described in Italy. The patient was a female, aged 37 years. The whole skin was affected except the face, neck, backs and palms of hands and soles of feet. Very good photographs are given of the atrophied wrinkled skin. Microscopically, in addition to the atrophy and loss of elastic fibres of the skin, a chronic granulomatous process was found characterised by an infiltration of round-cells and plasma-cells. In areas clinically normal, a progressive atrophy and inflammation were present microscopically. In this case Ducrey considers the cause as probably tuberculous. He obtained a positive focal reaction from the subcutaneous injection of 1 c.c. old tuberculin in a dilution of 1 in 10,000. R. C. L

SYPHILIS.

THREE CASES OF REINFECTION WITH SYPHILIS. P. Minassian. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. iii, p. 809.)

All three cases showed primary sores three or four years after being treated for syphilis. In two cases the first attack was treated in the primary stage and in one in the secondary stages. All were treated at the first attack with full courses of arsenic and mercury, and the second attacks were cured in the same way. R. C. L.

HECHT'S METHOD AND THE SACHS-GEORGI REACTION COMPARED WITH THE ORIGINAL WASSERMANN REACTION IN THE DIAGNOSIS OF SYPHILIS. A. Radaeli. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1921, fasc. v, p. 506.)

Radaeli found that Hecht's reaction, as usually carried out, gives results which, in 90 per cent. of the cases, coincide with those obtained by the original Wassermann. In some cases of undoubted syphilis Hecht's method was positive while the Wassermann was negative. This was especially the case in latent syphilis. Hecht's method may more readily than the Wassermann give positive or partial results in cases where syphilis might be excluded. It is recommended to supplement the original Wassermann. The Sachs-Georgi reaction gave similar results to the Wassermann in about 90 per cent. of cases, especially in cases of active syphilis with florid lesions. In cases of latent syphilis the method is less sensitive than the Wassermann. The Sachs-Georgi method also gives, more easily than the Wassermann, positive results in cases where syphilis might be excluded. The method has the advantage of a very simple technique, and can be practised where the original Wassermann is not available. R. C. L.

RESEARCHES ON THE VISCOSITY OF THE BLOOD AND ARTERIAL PRESSURE IN SYPHILIS. P. A. Meineri. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. v, p. 1013.)

The author found that in syphilis the viscosity of the blood is increased. This attains its maximum on the appearance of secondary manifestations. On treating the disease the viscosity of the blood diminished synchronously with the disappearance of the manifestations. In latent syphilis the viscosity is normal, but increases if syphilitic manifestations appear. The examination of the viscosity of the blood together with the serological and blood changes give information as to prognosis. Arterial pressure remains rather low when the viscosity of the blood is high and increases on the diminution of the latter.

R. C. L.

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY.

The 3rd Annual Meeting will be held at Liverpool, under the Presidency of Dr. Leslie Roberts, on Tuesday and Wednesday, July 10th and 11th, 1923.

The subjects chosen for discussion are:

(1) The physiological and pathological conditions governing the pattern and distribution of cutaneous reactions. To be opened by Dr. H. G. Adamson (London) and Dr. S. E. Dore (London).

(2) To what extent can the Wassermann reaction be depended upon as a guide to the diagnosis and therapy of syphilis? To be opened by Dr. Wilfrid Fox (London) and Dr. F. Wilson (Liverpool).

2nd CONGRESS OF FRENCH-SPEAKING DERMATOLOGISTS AND SYPHILOLOGISTS IN STRASBOURG.

The dates of this Congress will be July 25th to 27th, 1923, and not as stated in our previous announcement. The programme of subjects for discussion together with the names of the introducers has been announced in our issue of December, 1922 (p. 412). Those desiring to take part in the Congress should communicate with the President of the Organisation Committee, Prof. L. M. Pautrier, 2, Quai St. Nicolas, Strasbourg, before June 1st. The subscription is 60 francs.

The Congress will be preceded by the Congress on Cancer on July 23rd and 24th, and followed by the Conference on Leprosy on July 28th, 30th and 31st.

BOOKS RECEIVED.

Schäffer's Therapie der Haut- und Venerischen Krankheiten für Ärzte und Studierende. By Herbert Stranz (Breslau). 6th Edition. 1922. Berlin and Vienna: Urban & Schwartzenberg.

Venereal Disease in the American Expeditionary Forces. By George Walker, M.D. 1922. Baltimore: Medical Standard Book Co.

A Modern X-ray Department. London: Watson & Sons, Ltd.

THE BRITISH JOURNAL

OF

DERMATOLOGY AND SYPHILIS

JUNE, 1923.

CHRONIC URTICARIA AND ANGEIO-NEUROTIC ŒDEMA DUE TO BACTERIAL SENSITISATION.

H. W. BARBER, M.D., F.R.C.P.,

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In a previous communication (1) cases of chronic urticaria were described, in which the eruption was proved to be due to focal sepsis, and, as the association does not appear to be generally recognised, the publication in detail of some other cases of this kind is desirable. Judging from my own experience, I am now inclined to think that in the majority of patients, in whom chronic or recurrent urticaria, with or without angeio-neurotic symptoms, appears for the first time in adult life, the underlying cause is sensitisation to bacterial rather than to food proteins. The same is true, I believe, of asthma, and of that type of eczematous dermatitis which is apt to be associated with asthma. Food sensitisation has, I am convinced, been greatly exaggerated as a causal factor in asthma among adults, and I am unable to explain the number of positive cutaneous reactions towards food proteins obtained in these cases by the American school. While admitting the importance of sensitisation to animals—horse, cat, dog, and birds—I am in entire agreement with Dr. A. F. Hurst that it is exceptional in this country to obtain positive cutaneous reactions to foods in adult cases of asthma, although that type of child, who from his earliest days suffers from asthma, bronchitis, and a certain variety of eczema, usually gives very definite reactions to a number of foreign proteins. As the child grows older, however, I believe that it is bacterial sensitisation that comes to be the important factor, for immunity to food-substances is as a rule gradually acquired. Most American writers lay no stress on bacterial sensitisation as a cause of chronic urticaria, and in a

recent French text-book of dermatology it is not even mentioned, despite the fact that a great deal of work is being done in France on the relationship of urticaria to the phenomenon of anaphylaxis. On the other hand, Haldin Davis (2) states that " hidden sepsis is the most likely cause " of chronic urticaria.

The question of course arises why, since some degree of focal infection is so common as to be almost universal, pathological symptoms referable to it only occur in certain cases, and why such symptoms differ in different individuals. The problem is bound up with the phenomenon of sensitisation, and although, perhaps, everyone is capable of becoming sensitised to some toxin or other, some individuals and members of certain families are much more liable than others. Asthma, urticaria, angeio-neurotic œdema and certain forms of eczema may be looked upon as the outward and visible signs of sensitisation, and in their causation an hereditary susceptibility is undoubtedly often an important factor, and also a peculiar instability or hyper-excitability of the nervous system, which is easy to recognise clinically, but which we cannot at present define. In the case of bacterial sensitisation it will often be apparent that the sensitivity has developed during an acute infection, and if, after the subsidence of the acute attack, a local residual focus is left, in which the infecting organism to which sensitisation has occurred remains active, chronic or recurring symptoms of sensitisation, *e. g.* urticaria or asthma, are likely to develop. It is for this reason that foci of infection are of importance, apart incidentally from the fact that direct bacterial invasion of the blood-stream may take place from them. In the case of abscessed teeth, of a chronically inflamed appendix, and of suppuration in the nasal sinuses, even the most conservative advise removal of the focus of infection, but in the case of the tonsils the decision is not so easy. At the outset it cannot be too strongly emphasised that mere enlargement of the tonsils is no indication for their removal, and conversely that, if they are small, it does not follow that they are not a source of infection. Their enlargement in children, which is part of a general hyperplasia of the lymphoid tissue of the nasopharynx and pharynx, is doubtless due to chronic catarrhal infection, and this in its turn depends on improper feeding and unhealthy surroundings. The hyperplasia is a local defensive mechanism, and removal of the tonsils and adenoid vegetations, though sometimes advisable on mechanical grounds, will not ensure against recurrence of the infection, but, on the contrary, may predispose to it spreading down-

wards to the lower parts of the respiratory tract. The indiscriminate removal of tonsils and adenoids in early childhood that obtains at the present time is entirely indefensible. In older children and adults the state of affairs is different. Either as a result of severe attacks of tonsillitis, quinsies, or often *owing to a previous incomplete operation on the tonsils*, scarring may have occurred, the openings of several crypts may have been obliterated by scar-tissue, and actual abscesses may be present in the tonsillar substance. In several of my cases, in which the tonsils were a source of virulent infection, one or more operations had already been performed on them, and it cannot be too strongly insisted that anything short of complete enucleation is not only useless, but actually dangerous. In short, the tonsils are a source of infection if they contain septic matter—not merely concretions in the crypts, which are of little or no moment—shut up within their substance ; injection of the anterior palatal folds and of the tonsillar tissue, the presence of septic matter, and definite enlargement of, with attacks of painful swelling in the lymphatic glands draining the tonsils, are the main indications for their complete removal.

Just as asthma may be due to more than one variety of micro-organism, so an urticarial eruption may depend on sensitisation having occurred to a *Streptococcus longus*, the *Bacillus coli*, a *Staphylococcus aureus*, and possibly other bacteria. Probably a *Streptococcus longus* is most commonly responsible. One point of importance is that a previous history of rheumatic fever is not uncommon in these cases ; two of the patients in this series had it, and I have recently seen two others, who came to me for persistent urticaria, both of whom had chronic rheumatic valvular disease.

I have had a few cases in which the teeth were apparently the main source of infection, and in which recovery followed extraction of septic roots and treatment of pyorrhœa, with or without subsequent vaccination with an autogenous streptococcal vaccine. In one case a chronic appendicitis was almost certainly the cause. The patient, a woman, had suffered continuously for about eighteen months from severe urticaria, which the most rigid dieting failed to relieve. Careful examination disclosed no obvious course of infection, except a very tender appendix ; its removal two years ago was immediately followed by a most violent attack of the eruption, but since then there has been no recurrence. Oberndorf (3) also has reported a case of angeio-neurotic œdema, which yielded immediately to the removal of an inflamed appendix. By the courtesy of Dr. A. F.

Hurst I am permitted to reprint a most interesting case described recently in the *Practitioner*.(4)

Case 1 : *Urticaria following septic wound of thumb ; recovery fourteen years later after treatment with vaccine, made from streptococci isolated from a tooth.*— Miss M—, a nurse, aged 38 years, had a severely poisoned thumb in 1903, for which she was off duty for three months. She had never had any skin trouble, and had never suffered from asthma or hay-fever. About three months after her recovery urticaria appeared on the middle of the same forearm. It remained for a few weeks and then disappeared. After this it came and went, the attacks becoming gradually longer and occurring at shorter intervals, both arms being now involved. From October, 1919, to April, 1921, when she was admitted into New Lodge Clinic under Dr. Hurst's care, urticaria had been present in both arms without intermission.

She had experimented with almost every variety of food, omitting one after another from her diet for periods of a fortnight and sometimes of three or four months, but without benefit. For eighteen days she had taken nothing but milk, but the rash underwent no modification.

No obvious cause of the urticaria could be found, and the cutaneous reactions to the proteins of numerous foods and animal emanations proved negative.

The history suggested that the urticaria might be due to sensitisation to the organism which had caused her poisoned finger fifteen years ago, and that she had subsequently become infected elsewhere with this organism, at first intermittently and later continuously, and that the urticaria was a result of this sensitisation. She had had twenty-four teeth extracted in 1902 for abscesses round their roots, and her remaining teeth were found to be septic. The worst one was removed, and a streptococcus and *M. catarrhalis* were isolated from the granular tissue at the root.

On May 16th an autogenous vaccine containing five million streptococci was given. This caused a slight increase in the urticaria. Each subsequent injection caused a temporary aggravation of the urticaria, which improved in the intervals between the injections, together with pain in the arm, slight pyrexia, pain and, at first, discharge in the socket from which the tooth was removed, and with the larger doses *pain in the thumb and discharge from the wound*, which had been healed and free from pain for fifteen years.

The urticaria had greatly improved by July 15th, four days after the sixth injection ; during the next six days only three small spots were present. On August 15th it disappeared completely, but returned for a few days after each of the next ten injections. After the remaining two injections it reappeared only to a very slight extent, and since September 22nd there has been no trace of urticaria, except for a very slight return in November, which only lasted for four days.

Comments.—It will be noted that in this patient several teeth were removed for abscessed roots *four years before* the infection of the thumb occurred. The latter infection may have been *viâ* the blood-stream, *i. e.* a streptococcus from a remaining abscessed tooth may have infected

the thumb, possibly after local trauma, or, of course, the infection, may have been an external one. In any case the streptococcus in the teeth and in the thumb must have been of the same strain. Sensitisation to the organism presumably occurred during the acute infection of the thumb, and the presence of foci of infection with the same streptococcus in the teeth accounted for the persistent urticaria. The observation that, with autogenous vaccine treatment, pain in the thumb and discharge from the wound occurred fifteen years after it had healed is of enormous importance, illustrating as it does how long micro-organisms may remain latent in scar-tissue.

Case 2: *Chronic urticaria and angeio-neurotic œdema due to suppuration in the left antrum and frontal sinus.*—Mrs. H—, aged 46 years, consulted me in May of last year for the most violent urticaria with angeio-neurotic swellings, which appeared first in the previous February. Various changes of diet, purgation and sundry drugs had been tried without avail. The insomnia produced by the irritation had led to considerable exhaustion. As a child she had been very subject to colds, but of late had only had two or three every winter. Twelve years previously she had had a nasal discharge on the left side with tenderness over the left antrum, and she had since had an occasional bad smell in the nose. In December, 1921—two months before the onset of the urticaria—she had a heavy cold, and three weeks before she came to me she had another, which followed an injection of anticatarrhal vaccine, and was accompanied by sore throat and an intense exacerbation of the urticaria. She had recently had neuralgic pain over the left frontal region.

In ordinary routine examination I found muco-pus dripping from the left side of the nasopharynx, and there was some tenderness over the left fronal sinus. I therefore asked Mr. Zamora to see her, and he reported:

"*Tonsils* normal; *larynx* normal; *left antrum* opaque to transillumination."

Mr. Redding, on X-ray examination, reported:

"Greatly increased opacity of *left frontal sinus and left maxillary antrum*, indicative of empyema. The left ethmoidal cells show very slight loss of translucency, probably due to slight œdema of the mucosa. Right side normal."

Mr. Zamora operated May 18th, 1922. Intranasal drainage of the antrum and frontal sinus and scraping of the ethmoid region were performed. The antrum and ethmoidal cells drained well, but after a time there were again signs of retention in the frontal sinus. A second operation was undertaken, July 9th, 1922, the left frontal sinus being opened from the exterior and found to contain polypoid granulations, which were obstructing drainage to a certain extent. After this second operation the local condition recovered completely.

The uticaria became much less after the first operation, but returned when further retention occurred in the frontal sinus. It disappeared completely three days after the second operation, and she had not had another attack up to the time of writing.

Cultivations of the pus from the antrum and frontal sinus gave only a few

colonies of staphylococci, and no streptococci were found; it is probable, however, that a streptococcus was the original infecting organism.

Comments.—This case illustrates very well the importance of the nasal sinuses as a possible source of latent sepsis. Had I not happened to observe the muco-pus in the nasopharynx I should not have suspected sinus disease, as the patient made no mention of her previous nasal discharge until closely questioned. This is the only case of urticaria due to sinus infection that I have yet encountered, but I have three patients in whom lupus erythematosus was associated with chronic antral and ethmoidal infection.

Case 3: *A chronic erythemato-urticarial eruption associated with acute rheumatism; recovery after enucleation of the tonsils.*—Mrs. S. , aged 35 years, came to me in April, 1921, for a chronic erythemato-urticarial rash, which had appeared for the first time seven months previously and was attributed at the time to sea-bathing. She had suffered from recurrent attacks of tonsillitis as a child, and one preceded the outbreak of the eruption. Two months after its appearance (November, 1920) she had an acute attack of rheumatic fever, accompanied by sore throat, swelling of the joints, and high fever. At this time the rash was so severe that scarlet fever was suspected, and Dr. Goodall was called in consultation. He diagnosed acute rheumatism and considered the eruption to be a rheumatic erythema. After remaining in bed for six weeks she recovered from the rheumatism but the rash persisted. It appeared chiefly in the evening and after exertion or excitement, was intensely irritable, and, as its sites of predilection were the neck and shoulders, she was prevented from wearing evening dress. There is little doubt that the patient also had evening pyrexia at times, although she did not take her temperature. The pulse-rate even at rest was increased, and there was evident vaso-motor instability, as shown by alternate flushing and pallor of the skin. Various dietary experiments had been tried before I saw her, but without effect.

The history of repeated sore throats in childhood, the fact that the outbreak of the eruption was preceded by sore throat, as was also the attack of rheumatism, and that during the latter the rash was very intense, suggested to me the probability that sensitisation to a streptococcus had occurred, the eruption being a manifestation of this. Everything pointed to the throat being the source of infection, although at first sight it was not obviously septic. *The teeth* appeared in good order, but no radiograms were taken. Careful examination showed that the tonsils were scarred and definitely septic, and a *right tonsillar gland* was much enlarged and slightly tender. There was no evidence of appendicular or gall-bladder infection, and the lungs and heart were normal. Cutaneous tests to *stock* proteins of *Streptococcus viridans*, *S. non-hæmolyticus* and *S. hæmolyticus* were negative.

At my request Mr. Zamora examined the patient and reported that there were no signs of sinus disease, but that the tonsils were clearly a possible source of infection. The rational line of treatment seemed to be enucleation of the tonsils,

followed, if necessary, by the giving of autogenous streptococcal vaccine prepared from them with a view to "desensitising" the patient.

Enucleation of the tonsils was performed on May 1st, 1921; the operation was followed by a profuse outbreak of the rash and considerable pyrexia. The temperature remained raised for about ten days—an unusual thing after this operation. The patient went away to the sea, and returned much improved in general health. She no longer felt as though she had fever in the evening, and the vaso-motor instability was not so marked. The rash, though very much less, still appeared slightly from time to time, and it was decided to give a course of autogenous vaccination with organisms cultured from the tonsils. These were a *Streptococcus longus*, which greatly predominated, and a *Micrococcus paratetragenus*. *An intradermic test with the vaccine prepared was definitely positive*; a control, using stock staphylococcal vaccine, was negative.

About twelve injections were given in increasing doses. They appeared to have two definite effects—one to provoke a slight outbreak of the urticaria, the other to cause *the enlarged right tonsillar gland to swell up and become tender*. This focal reaction in the gland occurred after several, but not all the injections, and became progressively less. The patient has now been free of the eruption for over a year, and her general health is excellent.

Comments.—In this case there was a history of repeated sore throats, and sensitisation to the infecting organism—a *Streptococcus longus*—presumably took place during the attack which preceded the initial outbreak of urticaria. Enucleation of the tonsils was considered advisable because (1) they were scarred and septic, (2) a right tonsillar gland was enlarged and tender, (3) the patient had had an attack of acute articular rheumatism, and (4) there had evidently been continuous evening pyrexia suggesting constant infection from this, the only source apparent. The slight persistence of the urticaria after operation was doubtless due to the existence of a secondary focus in the enlarged right tonsillar gland; the focal reaction in this gland alone makes this almost certain. It is the presence of such secondary foci in lymphatic glands and probably in the intestines that doubtless accounts for the persistence of symptoms of infection when main and primary foci, such as teeth and tonsils, have been removed. It is important to note that cutaneous tests with stock streptococcal proteins were negative, whereas an intradermic test with the patient's own vaccine was positive. Owing to the specificity of different strains of bacteria, cutaneous tests with stock bacterial proteins are seldom in my experience of any value.

Case 4: This case was strikingly similar to the last, but the urticarial eruption was, when at its worst, accompanied by angeio-neurotic swellings.

Mrs. A—, aged 30 years, was brought to me in consultation in January of last year on account of recurrent urticaria, which began in the form of occasional

attacks at the age of twenty. She had had rheumatic fever at the age of thirteen, and was in bed with swelling of the joints for some six weeks. Her teeth were all removed in 1914, and in the same year her tonsils were operated upon on account of repeated sore throats. Early in 1918, when in America, her attacks of urticaria became very severe, and on returning to England she was operated upon by a well-known gynæcologist for pyosalpinx, and was told that it was unlikely she would ever bear children. She remained comparatively free from urticaria for some months after this operation, but later the attacks returned. She was then treated by a bacteriologist with injections of vaccine prepared from the fæces (? *B. coli* vaccine), and of iron and arsenic. This treatment brought about improvement in her general health, and her urticaria was less severe. At Christmas, 1921, however, she had a most severe attack, with high pyrexia and intense swelling of her face, so that she was unrecognisable; it began "as though she had influenza," with shivering and pains all over, and she had noticed similar symptoms with previous severe attacks. Needless to say attempts had been made to incriminate various articles of food, but it was found that dieting made little or no difference, and she was never able to associate the severe attacks with any particular food-substance.

The patient was a fair-haired, healthy-looking woman with the same tendency to sudden flushing and pallor as was remarked in the case just described. *The teeth* were all false. *The tonsils*: Although tonsillectomy had been performed seven years previously, only the upper poles had been removed, and the lower poles were large and lobulated, extending far down the pharynx; the tonsillar glands were enlarged. The patient had noted that these glands sometimes swelled and became slightly painful. Examination of the chest and abdomen revealed nothing abnormal.

The fact that the severe attacks of urticaria were accompanied by febrile symptoms and definite pyrexia, and that they appeared to bear no relationship to diet, seemed to point to some latent infection being the cause. The history of rheumatic fever in childhood and of repeated sore throats, and the fact that the tonsil operation had left scarred remains, made me suspect a throat infection as the original cause of bacterial sensitisation having occurred, and the tonsillar remains as a possible source of infection. On the other hand, we had to consider the apparent improvement that had followed the operation for pyosalpinx and also the injections of fæcal vaccine. For this reason it was considered advisable to have a complete pelvic examination made, and to investigate the fæcal flora. The former revealed no evidence of latent pelvic infection, and no abnormal organisms were found in the fæces. The urine was also normal. Moreover, Mr. Skene Keith found the complement-fixation test to the gonococcus completely negative.

Cutaneous tests performed with stock proteins of streptococci (three types), pneumococci (three types), *Micrococcus catarrhalis*, *B. coli*, *M. tetragenus*, *Staphylococcus aureus*, *albus* and *citreus*, and an intradermic test with stock gonococcal vaccine were all negative.

Mr. Zamora reported that the tonsillar remains were a possible source of infection, but he was doubtful whether they were sufficient to account for the urticaria. The position was put to the patient and she decided to have the tonsils completely enucleated. The operation was performed immediately, an opportunity being also taken, while the patient was under the anæsthetic, of

again examining the pelvis, with negative result. There was considerable hæmorrhage from the throat some hours after the operation, but this was controlled. Some days afterwards an attack of urticaria with swelling of the face and buccal mucous membrane developed, but rapidly subsided, and the patient went away to the sea to convalesce.

Since then there has been no recurrence whatever of urticaria and no febrile attacks. The patient has put on weight considerably and states that she is in better health and condition than she has been for years. All she complains of is a tendency to flushing of the skin of the face and neck when excited, but this is obviously merely a patchy erythema of psychical origin common in women of a certain temperament.

The enucleated tonsillar remains were examined bacteriologically, but only a few colonies of *Staphylococcus aureus* were obtained. It was subsequently found, however, that the incubator was out of order, and that the temperature rose to 42°–46°C. Later swabs were examined from the tonsillar beds, and a long-chained non-hæmolytic streptococcus, together with a *Streptococcus brevis* and staphylococci were obtained.

Comments.—This case is, perhaps, less convincing than Case 3, and yet, in spite of the most careful search, no other source of infection but the scarred tonsillar remains was discovered, the tonsillar glands were enlarged and became periodically swollen and tender, there was a history of rheumatic infection, and removal of the tonsillar remnants has not only led to a cessation of the urticarial attacks, but has been followed by great improvement in the patient's general health.

Case 5: Miss M. C—, aged 31 years, came to see me in April of last year for chronic urticaria, with attacks of swelling of the eyes and lips, dating from an acute attack on New Year's Eve. She had had pneumonia of the right lung at Christmas, 1920, and was subject to frequent colds and sore throats. During the air raids her thyroid gland became swollen, but later subsided. She complained of being easily tired. Changes in her dietary had had no apparent influence on her urticaria. On examination there were numerous urticarial wheals, chiefly on the chest, abdomen and thighs. The face and neck were flushed, there was no exophthalmos, the thyroid gland was rather full, the pulse-rate was 114, and there was obvious hyperidrosis of the face and hands. There were no signs of organic disease of the heart and lungs, though the heart-beat was rather tumultuous, and abdominal examination was negative. *The teeth* were in good condition; three were false. *The throat* was acutely inflamed, the anterior pillars of the fauces were injected, and there were yellowish patches on the posterior pharyngeal wall. *The tonsils* were swollen, injected, and contained septic material. There were neither symptoms nor signs of nasal sinus infection. I advised the patient to see Mr. Mollison, who thought enucleation of the tonsils advisable. He operated in May. Ten days after the operation she had a mild outbreak of urticaria on her face and chest, and another slighter one a fortnight later. Since then she has been entirely free from her eruption. The left side of the thyroid gland is, however, now considerably enlarged, and the flushing,

tachycardia and hyperidrosis are still evident. It is probable that this unilateral enlargement is adenomatous, and the patient has been advised to seek expert advice for its treatment. The enucleated tonsils were not examined bacteriologically in this case.

In all probability the infecting organism responsible for the urticaria in all these cases was a *Streptococcus longus*, but it must be remembered that *B. coli* infections, *e. g.* pyelitis and cholecystitis, may produce urticaria, and the following case shows that a *Staphylococcus aureus* may provoke an urticarial reaction, should sensitisation to it occur.

Case 6: Miss C—, a middle-aged lady, was referred to me by Dr. Mutch, under whose care she was for chronic rheumatism. Some time previously she had had a large carbuncle on her left thigh, which had left a scar of considerable size. Shortly afterwards she began to develop crops of boils at intervals, chiefly around the vulva and perinæum. *With each fresh crop of boils a ring of urticarial wheals would appear around the scar of the carbuncle*; so constant in its conformation and development was this urticarial reaction that the patient termed it her "fairy ring."

It would seem clear that the area of skin at the original site of the carbuncle had become sensitised to the *Staphylococcus aureus*—probably some active organisms were still present in the scar—and that with each fresh infection in the form of boils a localised urticarial response occurred in the sensitised area. Treatment with an autogenous staphylococcal vaccine was successful in bringing about a cure of the boils, and the urticarial ring ceased to appear.

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ADULT URTICARIA PIGMENTOSA.

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Dr. Wallace Beatty's clinical note on a case of adult urticaria pigmentosa in this journal of April, 1921, gives a precise picture of an apparently not very well known though perhaps not very rare affection of the skin, which, apart from its intrinsic interest as a clinically very definite and characteristic adult type of pigmentary urticarial eruption, has a practical importance in that it is often mistaken for a secondary syphilide. The question of its possible relationship to the better known urticaria pigmentosa of children is also of interest.

Several of these cases have been shown at meetings of the Dermatological Section, and on each occasion there has been a discussion as to whether they constitute a separate affection or are a variety of urticaria pigmentosa. The first of these cases was exhibited by Dr. Douglas Heath in 1913 as a case for diagnosis. The patient was a young medical man, and the brown pigmented areas, $\frac{1}{16}$ to $\frac{1}{8}$ in. in diameter, over the trunk and limbs had been present for 2 years. They became slightly raised when rubbed. Dr. Whitfield recalled two similar cases, but doubted whether they were genuine urticaria pigmentosa, and thought they were a disease *sui generis*.

In 1914 I showed the case of a stoutish woman, A. B—, aged 44 years, with the diagnosis *generalised lentiginous pigmentation in an adult*; (?) *adult urticaria pigmentosa*. A photograph of this case was published in the *Transactions of the Royal Society of Medicine* (April, 1914, Derm. Sec., p. 104) and presented the appearance of profusely distributed small lenticular macules, very similar to that of the case depicted in the photograph accompanying Dr. Wallace Beatty's note, and to that in a paper by Kerl in the *Archiv f. Derm. u. Syph.*, cxviii, September, 1913 ("a note on pigmented types of urticaria").

Dr. Whitfield considered this a case of an unnamed disease distinct from urticaria pigmentosa, and mentioned a similar case in which a biopsy

was made and the characteristic mast-cell infiltration was not found. A microscopical examination of a lesion of my case showed only a few mast-cells—not more than in any inflammatory cell exudation.

I noted at the time of showing this case (A. B—) that I had observed other similar cases, and I shall now give a brief description of some of these cases in order to demonstrate their similarity.

Eliz. G— (July 26th, 1912), aged 50 years, housework. A stout woman whose urine contains a trace of sugar. The eruption appeared 18 months ago as "white blisters" (*i. e.* wheals), which were gradually followed by small brown patches. Fresh wheals and brown stains have continued to appear and now there is a profuse eruption of split-pea-sized reddish-brown macules over the whole body, except on the face and palms and soles, and most abundantly on the flexor surfaces of the limbs. The red colour fades on pressure and leaves a yellow stain. There is some itching, but it is not intense. On friction the macules become turbid, but there is no dermographism.

Mrs. B—, aged 52 years, married (October 8th, 1913). A stout woman. The eruption began 4 or 5 years ago on the arms and breasts, but it has only lately become profuse. Now there are very numerous brown macules on the arms, forearms and breasts. There are some on the abdomen and back and a few on the legs. They are oval, reddish-brown macules of the size of a split-pea. Most are quite flat, but some are slightly raised and more red than the flat macules. The redness fades on pressure and leaves a yellow stain. They do not itch. They swell slightly on friction. There is no dermographism and no urticaria. Ten years ago she had a very severe attack of urticaria. Patient is in good health, but is getting stouter. No sugar in the urine.

Thus my first three cases were in stout women and I began to regard this as a feature of the complaint, but my fourth case was, like Dr. Douglas Heath's case, in a healthy young man.

A. K. S—, male, aged 22 years. Eruption present 3 or 4 years. Numerous small rounded and oval freckle-like macules, most abundant on the trunk, arms, backs of hands, thighs, calves, and dorsal surfaces of feet. It does not itch at all, but friction causes the macules to swell slightly and thus to become a little raised. Some are dark brown (a few almost black), some pale brown and some reddish-brown. During examination a group of 3 or 4 small oval wheal-like swellings of the same size as the macules, but in between, not on them, appeared on the chest.

This patient had just previously been rejected as a candidate for a post in a government office on account of the eruption, which was regarded as syphilitic.

Another case, in a young woman, F. S—, I was asked to see in the Maternity Ward on account of a profuse eruption of brown freckle-like macules, chiefly on the arms and legs, but also on the trunk, which was suspected to be a secondary syphilide. Ten months later the eruption was quite unchanged. No itching was complained of, but there was swelling of the macules on friction.

In none of these cases was there much itching or marked urticaria, and sometimes these seemed to be absent. A few spontaneous small urticarial wheals were seen at one examination in the case of the male patient. Even a factitious urticarial swelling of the macules on friction was sometimes recognised only by close observation.

But in a case exhibited by Dr. Dore in 1915 (*Brit. Journ. Derm.*, xxvii, p. 426), *urticaria pigmentosa in an adult*, in a strong, healthy-looking man, aged 31 years, there was intense pruritus and marked factitious urticaria accompanied by a macular pigmentary eruption on the trunk, upper arms and thighs, which had existed for 8 years.

In a case by Dr. Graham Little (*Brit. Journ. Derm.*, 1916, xxviii, p. 327) in a man, aged 35 years, the eruption had been present for 19 years, and consisted of small red and reddish-brown stains thickly distributed over the wrists, forearms and arms, and less extensively on the trunk. The macules were $\frac{1}{4}$ in. in diameter and became turgid and vividly red on rubbing. There was considerable factitious urticaria, but little spontaneous itching.

Darier, in "Some Remarks on Urticaria Pigmentosa" (*Annales de Derm. et de Syph.*, 1905, p. 339), mentions some adult cases in which there was no dermographism and no itching even with the well-marked urticarial reaction which could be induced in the macules by rubbing.

Wallace Beatty's case was in a gentleman, aged 32 years. There was factitious urticaria easily provoked on friction, but only very slight itching after a bath.

If we sum up these cases we find :

(1) That the affection begins in adult life in either sex.

(2) That it may last for many years (Beatty's case 10 years, Little's case 19 years).

(3) That the eruption consists of small freckle-like macules about

$\frac{1}{8}$ to $\frac{1}{4}$ in. in diameter, more or less profusely over the trunk and limbs, but not on the face or hands or feet.

(4) That on friction the macules become red and slightly raised from urticarial swelling.

(5) That itching, urticaria, dermographism may be very slight; less often (as in Dr. Dore's case) itching may be intense and urticaria well marked.

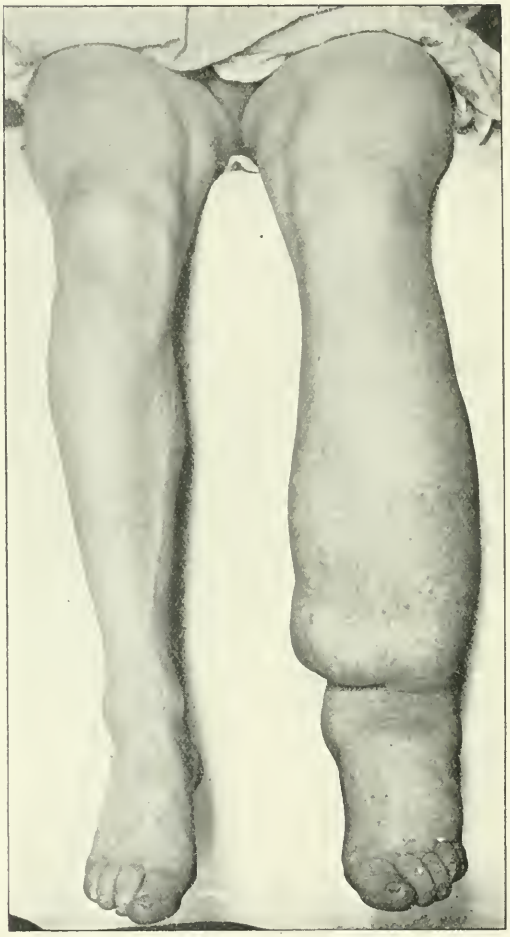
(6) That the eruption is frequently mistaken for a secondary syphilide.

In no case have large macules or nodules been seen such as are characteristic of urticaria pigmentosa in children, so that clinically the adult form of pigmentary urticaria is at any rate a distinct type. As to whether it is to be regarded as the same or a separate disease would seem to depend upon the finding or not finding of mast-cells in abundance. Records as to these findings vary:

Whitfield's case . .	No mast-cells.
My own case . .	Very few mast-cells.
Dore's case . . .	Large numbers of mast-cells.
Little's case . . .	Enormous increase of mast-cells typical of urticaria pigmentosa.
Wallace Beatty's case .	Closely set mast-cells in cutis.
Drummond's case (quoted by Beatty) .	Abundance of mast-cells in corium.

Kerl states that in the adult type there are no mast-cells.

Possibly the presence of mast-cells may depend upon the degree of urticarial element.



Elephantiasis nostras of left leg.

TO ILLUSTRATE DR. PARKES WEBER'S ARTICLE ON "IDIOPATHIC" ELEPHANTIASIS NOSTRAS OF LOWER LIMBS AND ITS RELATION TO TROPHŒDEMA AND MILROY'S DISEASE.

A NOTE ON "IDIOPATHIC" ELEPHANTIASIS NOSTRAS OF LOWER LIMBS AND ITS RELATION TO TROPHŒDEMA AND MILROY'S DISEASE.

F. PARKES WEBER, M.A., M.D., F.R.C.P.

The following case is an excellent example of the kind to which I wish specially to refer. The patient, J. B—, was a man, aged 64 years, who had never been out of England, and who sought advice in regard to the condition of his left lower extremity, a condition which is well shown in the accompanying illustration (see figure). The change was limited to the parts below the knee and was apparently due to a chronic increase or hyperplasia of the subcutaneous connective tissue—a form of "elephantiasis nostras" of uncertain causation, that is to say, of so-called "idiopathic" nature. The main swelling was just above the ankle, which in the illustration is seen to be overhung by a projecting flounce-like collar of the hyperplastic tissue of the lower part of the leg. The condition had gradually developed in the course of the past seventeen years. He had had pain, he said, in the affected leg, but had never had any ulcer or erysipelas-like attack. The skin over the swelling was still fairly smooth ("elephantiasis glabra"); it was only commencing to show the "coarse" appearance usually noted in similar cases. There was no offensive smell from decomposing cutaneous secretion, such as is often met with in cases in which the surface of the skin has become uneven and "warty." The patient had never had syphilis, and I do not think that there was a history of any similar condition in other members of the patient's family.

In 1921 I saw a woman, aged 57 years, with a very similar condition of "elephantiasis nostras" of the right lower extremity, which, she said, had commenced at about 30 years of age, after an injury. But the injury must have been a slight one, for she seems not to have been confined to her bed for more than two or three days after it. In extreme examples of the same class the collar-like swelling of the subcutaneous tissue around the ankle may become so great as completely to overhang and more or less to hide the foot, so

that E. C. Bousfield termed the condition in his remarkable case one of "hidden foot" or "cryptopodia."* His patient was a woman, aged 44 years, in whom a collar-like swelling of the subcutaneous tissue around the ankles, which commenced as œdema at 15 years of age, had gradually become so excessive as completely to hide both feet, including the toes.

These cases seem to me to be due to a gradual hyperplasia of the ordinary white connective-tissue elements in the subcutaneous tissue of the affected parts, which at the commencement may be associated with more or less true subcutaneous œdema and definite "pitting" on pressure. There seems in these cases to be a deficiency in true cutaneous elasticity, with or without absolute or relative hypoplasia, deficiency, or degenerative change in the elastic elements, so that as a result of the connective-tissue hyperplasia combined with deficiency in true cutaneous elasticity, the skin and subcutaneous tissue tend to become "baggy," or to fall in a pouch-like or flounce-like manner over the parts of the body below it, thus constituting a non-elastic kind of dermatolysis—one form of so-called "dermochalasis," "chalasodermia," "chalastodermia," or "chalodermia" (the term used by Ketly).

The skin of the affected parts tends gradually to lose its normal appearance, and often assumes a "coarse," pitted or "warty" surface. Sometimes the patients suffer from recurrent erysipelas-like attacks of erythema of the affected parts, possibly due to exacerbations of some chronic secondary infection of the skin. But this infection must not be regarded as the primary cause of the whole condition; there was, indeed, no history of such erythematous attacks in the first case (the man, J. B—) in the present paper.

The condition of dermatolysis, above referred to, is sometimes associated with the presence of definite molluscous fibromata—of the type met with in Recklinghausen's disease—and is then doubtless allied to the class of "pendulous" fibrous tumours. Such cases must be distinguished from the neuromatous form of "pachydermatocele" —"elephantiasis neuromatosa" or "elephantiasis neurofibromatosa" —in which there may be actual plexiform neuroma together with more or less general connective-tissue hyperplasia of the affected part.

* E. C. Bousfield, "Cryptopodia: an Undescribed Disease," *Lancet*, London, 1919, ii, p. 329.

But some of the neuromatous cases are doubtless also allied to Recklinghausen's disease.

Amongst the cases described under the heading "pendulous tumours" or "dermatolysis" (not the "movable" or "elastic" skin kind of dermatolysis) are some wonderful examples in which large folds of coarse skin containing fibromatous connective-tissue masses hang from the scalp over the side of the head, from the temple, eyebrow and forehead over the eye and cheek, or from the flank, hip and buttock over the thigh, etc. In H. Radcliffe Crocker's *Atlas of Diseases of the Skin* (1896, ii, plate 73, fig. 2) a huge tumour of the kind is illustrated. It hangs from the side of a man, who has many molluscous fibromata. A still more remarkable case of fibromatous thickening of the skin and "dermatolysis" was described and figured by Ladislaus von Ketly in 1901, under the heading of "a peculiar change in the skin (loose skin)."* The patient in question was a female cook, aged 30 years, and the thickened skin hung in folds or "flounces" about the thighs, as if it were slipping down. The famous "elephant man," who was demonstrated at the Pathological Society of London by Sir Frederick Treves,† had, besides his bony abnormalities, etc., fibromatous tumours and lax masses of pendulous skin. Radcliffe Crocker‡ described a man, aged 39 years, in whom "enormous pendulous folds of skin and subcutaneous tissue, overlapping like flounces, depended from the twelfth rib to about halfway down the thighs." In another case also referred to by Crocker, and, like the preceding one, not congenital, a somewhat similar condition of hyperplasia of connective tissue, "but less developed, and not so lax, was limited to the palms, soles, sides of neck, nose and tonsils, in the last part necessitating excision." A case of "elephantiasis nostras" of the vulva in a woman, aged 23 years, which I recently described,§ probably belonged (whether there was a scrofulous basis or not) to the same class of diffuse connective-tissue hyperplasia of the skin and subcutaneous tissue.

* L. von Ketly, "Ein Fall von eigenartiger Hautveränderung—Chalodermie (Schlaffhaut)," *Arch. f. Derm. u. Syph.*, Wien, 1901, lvi, p. 107.

† Sir Frederick Treves, "A Case of Congenital Deformity," *Trans. Path. Soc. Lond.*, 1885, xxxvi, p. 494. See also Treves, *The Elephant Man and Other Reminiscenees*, London, 1923.

‡ H. Radcliffe Crocker, *Diseases of the Skin*, 3rd edition, 1903, pp. 885–886.

§ F. Parkes Weber, *Brit. Journ. Derm. and Syph.*, London, 1923, xxxv, p. 106.

Allied to this class are probably also the rare cases of "primary (non-septic) diffuse hypertrophy of the gums." This is confirmed by the occurrence of diffuse hypertrophy of gums in the remarkable family series of cases of molluscous fibromata* described by John Murray in 1873, and afterwards by A. Whitfield and A. H. Robinson in 1903.

Here I would refer to certain cases of congenital "elephantiasis" of the legs and various parts similar to the acquired non-parasitic cases in adults. M. Mainzer† wrote about a girl, aged 4 years, with what he described as congenital "elephantiasis" of the left upper extremity, both legs, the right foot and the external genitals. Mainzer alluded also to other cases of congenital elephantiasis of adult type described by Reinbach, Spietschka, Nonne, Moncorvo, Miram, and Koch, and a Russian case recorded in 1864. Spietschka's case was that of a girl, aged 10 years, with congenital "elephantiasis" of both legs, the right arm, the external genitals and the face. In some of the cases there were circular congenital grooves in the limbs, and the results of "intra-uterine amputations."

The first cases described in this paper, in which one lower extremity or both lower extremities were involved, bring me to the cases of so-called "trophœdema" and "idiopathic œdema," sometimes congenital and sometimes familial, leading gradually to permanent enlargement and a kind of "elephantiasis nostras" of extremities—generally one or both lower extremities. Familial cases have been described under the heading "Milroy's Disease,"‡ and earlier by M. Nonne, as "Elephantiasis Congenita Hereditaria."§ Advanced cases of troph-

* *Medico-Chirurgical Transactions*, London, 1873, lvi, p. 235, and 1903, lxxxvi p. 293.

† Mainzer, "Ein Fall von Elephantiasis Congenita," *Deutsch. med. Woch.*, 1899, xxv, p. 436.

‡ W. F. Milroy, "An Undescribed Variety of Hereditary Œdema," *New York Med. Journ.*, 1892, lvi, p. 505; Sir H. D. Rolleston, "Persistent Hereditary Œdema of the Lower Limbs," *Lancet*, London, 1902, ii, p. 805; W. B. Hope and H. French, "Persistent Hereditary Œdema of the Legs," *Quart. Journ. Med.*, Oxford, 1908, i, p. 312; J. D. Rolleston, "Persistent Hereditary Œdema of the Legs (Milroy's Disease)," *Rev. Neur. Psych.*, Edinburgh, 1917, xv, p. 480. See also the copious French literature by H. Meige and many others on the subject of trophœdema, including congenital and familial examples.

§ M. Nonne, "Vier Fälle von Elephantiasis Congenita Hereditaria," *Virchow's Arch.*, 1891, cxxv, pp. 189–196, with plates 4 and 5. There can be no doubt that Nonne's cases are of the same kind as those later on described by Milroy, etc.

œdema seem generally to suffer from occasional exacerbations of the swelling, with redness of the kind to which I have already alluded, but it must not therefore be supposed that a recurrent erysipelas or streptococcal infection is the cause of the whole condition, though recurrent streptococcal lymphangitis may cause persistent swelling and "elephantiasis," that is to say, an apparently similar condition, in some cases.

Isolated examples, without familial history, seem mostly to have been in women, commencing in early adult life. I have observed two or three such cases. In a young woman, aged 23 years, whom I showed at the Royal Society of Medicine, Clinical Section, on December 11th, 1908,* the œdema (left leg) seemed to have been of congenital origin. In a woman, aged 29 years, whom I showed at the Medical Society of London in 1912,† the œdema (right leg) first appeared at the age of about 27 years.

On comparing the illustration of the legs in J. B— (the man whose case I referred to at the commencement of this paper) with the illustrations of legs in late cases of Milroy's disease,‡ one notices a certain resemblance, but the connective-tissue hyperplasia and "bagging" about the ankles seem generally to be less marked in Milroy's disease (and trophœdema).

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

Meeting held on January 18th, 1923, Dr. H. G. Adamson, President of the Section, in the Chair.

Dr. E. G. Graham Little showed a case of *keloid after burns*. The patient, a boy, aged 11 years, received a burn eight months ago, and a keloidal growth had taken place on the site of the burn, and now covered almost all the middle surface of the thigh. An interesting feature was that part of the large patch had undergone spontaneous healing. The history was very precise, namely, that the fenestrated areas which were now, apparently, unaffected, had been keloidal, and the upper margin of

* F. Parkes Weber, *Proc. Roy. Soc. Med.*, Clinical Section, 1908–1909, ii, p. 52.

† F. Parkes Weber, *Trans. Med. Soc. Lond.*, 1912, xxxv, p. 370.

‡ See illustrations in the papers on the subject referred to in a previous footnote.

the keloid was marked by a little isolated lesion on each side of the thigh. At the same time parts of the tumour formation were extending in the typical crab-like way, so this presented a remarkable combination of the retrocessive and the advancing types of the affection. He proposed to have the main area treated with radium, because it was very itchy and painful, and the boy's rest was badly disturbed by it.

Dr. Henry MacCormac showed a case of ? *idiopathic hæmorrhagic sarcoma of Kaposi.* The patient, a man, aged 59 years, developed the condition seen on the feet two years ago. Some years previously he had had phlebitis, but an interval elapsed during which the lower extremities remained to all outward appearances normal. The present eruption was confined to the feet. On the dorsal surface there were superficial ulcerations or abrasions; they were not extensive, and probably arose from coccal infection. All the toes of both feet were distinctly swollen and "infiltrated"; the degree of congestion was considerable at times, rendering them almost plum-coloured. During the summer the lesions on the toes lessened in degree, but never disappeared. It was interesting to note that the patient was of Semitic origin and came from Galicia—two points which, taken in conjunction with the morbid appearances, suggested the possibility of a hæmorrhagic sarcoma.

Dr. J. M. H. MacLeod said that this condition appeared to him to be more like a varicose ulceration, due to some obliterative condition of vessels, than a hæmorrhagic sarcoma.

Dr. J. H. Sequeira remarked that he did not see any striking resemblance to the so-called hæmorrhagic sarcoma. In the cases he had seen there had always been a chronic purplish congestion of the extremities in addition to the formation of nodules, and in one patient still under observation, who was shown at the International Congress in 1913, the purplish congestion had persisted throughout, and the granulomatous nodules had been more of the nature of an epi-phenomenon. The late Sir Jonathan Hutchinson originally described the condition as chronic symmetrical purplish congestion of the extremities. This patient's upper extremities were free. Histologically the condition was inflammatory, and was best described as an angiomatous granuloma. Dr. MacLeod's suggestion was a more probable diagnosis.

Dr. Henry MacCormac showed *two cases for diagnosis.* Case 1: A boy, aged 14 years, had had the present condition for four months. The eruption began on the chest, and gradually spread, so that it was now extensively distributed over the thorax and abdomen, upper and lower arms and thighs, and was present to some extent on the face. There were no subjective sensations, and no lesions had been found on the mucous

membrane; the lymphatic glands were not enlarged. Some of the lesions were small maculæ with scaling; some were distinctly papular.

Case 2: A girl, aged 18 years, with a similar eruption. In her case the lesions first appeared six months ago, were profuse, and distributed in an identical manner. The greater part of the eruption was of the erythemato-squamous type and probably none of the lesions were papular, although in some the suggestion of a papular nature was conveyed to the observer. The elbows and knees were not affected.

In both cases the Wassermann reaction was negative.

These two cases presented a peculiar erythemato-squamous eruption, four examples of which had recently come under the exhibitor's observation. In the first two cases seen the lesions completely cleared up after remaining present for from four to six months, and he thought in the present cases a similar course would be pursued. It might be added that the second (female) patient was admitted with a diagnosis of psoriasis. Treatment seemed to have but little effect on the lesions, and judging by the cases previously seen it would appear that the eruption followed a prolonged course, in time disappearing spontaneously.

Dr. J. H. Stowers inquired why Dr. MacCormac doubted the seborrhœic origin of these cases, as, in his opinion, they were of that nature.

Dr. H. G. Adamson (President) thought that both were cases of acute psoriasis

Dr. Haldin Davis regarded both these cases as belonging to the group of pityriasis lichenoides chronica. He could not agree with the view that they were psoriasis. He did not think that any case, even of acute psoriasis, would last so long as these had—five or six months—without an increase in size of the individual lesions or without showing any tendency of the lesions to coalesce. Moreover, it was not possible to get a typical psoriasis scale off any of the lesions. He also thought that the long duration of the cases proved that they were not pityriasis rosea.

Dr. Barber agreed with Dr. Haldin Davis in regard to the second case.

Dr. Douglas Heath expressed his agreement with Dr. Stowers' views.

Dr. Graham Little said he had recently seen a case like these, but with a much longer history, namely, some years. In that case his confident diagnosis was parapsoriasis, and he would have diagnosed the present two cases as such but for this experience. His own case cleared up completely with nothing but local treatment, and the ultimate diagnosis was that of psoriasis.

Dr. MacCormac (in reply) said he had only recently seen the boy. He made a section from one of the lesions in the case of the girl. It was not typical, but it suggested psoriasis.

Dr. J. H. Sequeira showed *two cases illustrating the benefit of light baths*

in tuberculous disease of the skin.—(These cases have been described in Dr. Sequeira's article in the March number of this Journal, p. 93.)

Dr. E. G. Graham Little showed a case of *very extensive sclerodermia.* The patient, a woman, aged about 40 years, had had a progressive sclerodermia for several years, which had advanced to occupy large areas of the chest and back of the trunk, the abdomen, and thighs. The disease had rapidly improved apparently as a result of the extraction of her teeth, which were pronounced to be septic. This case was reminiscent of the very extensive case of sclerodermia which he showed to the Section several years ago,* that of a lady who had been under the care of Sir Thomas Barlow, and who had also rapidly improved out of all recognition as a result of the extraction of all her teeth.

Dr. Louis Savatard showed a section from a case of *ulcus rodens erythematoides.* He said that in October last Dr. Adamson showed at a meeting of the Section a case of "Multiple Superficial Rodent Ulcer: possible Embryonic Sweat-duct Origin," and demonstrated microscopical sections of the growth to support this theory of origin. Dr. Savatard now showed sections of a similar case which clearly demonstrated a sweat-duct passing through the button-like masses of basal cells. The tumour-cells took the hæmatoxylin stain more readily than did the duct-cells, and under a high power could easily be differentiated. He suggested that Dr. Adamson's sections simply showed the involvement of sweat-ducts in the growths.

Dr. Savatard also demonstrated slides and sections of the following cases:

(1) Peri-articular Cystic Fibromata of the Skin (the so-called "synovial" tumours of American writers).
(2) Multiple Sebaceous Carcinomata.
(3) Early Spino-basal-celled Carcinoma (Darier).

Mr. J. E. R. McDonagh read a paper on *manganese as a chemotherapeutic agent.* (The paper was published in full in the March number of this Journal, p. 98.)

Dr. H. G. Adamson (President) confessed that he found it very difficult to follow Mr. McDonagh's arguments clearly. Many of his theories were not supported by sufficient evidence, but he (the President) was not really competent to offer any material comment, and he would be glad to hear remarks from others, particularly from those who were more conversant with biochemistry.

* *Proc. Roy. Soc. Med.* (Derm. Sect.), 1916, ix, p. 69.

As regards the practical side, he congratulated Mr. McDonagh upon having obtained in the long list of cases of different types of coccic infection the good results with manganese butyrate which his theories had led him to expect. He hoped that these good results would be confirmed by the experience of others, and that manganese butyrate would prove to be of the value in the treatment of lupus vulgaris which was predicted for it.

Dr. A. M. H. Gray said he did not pretend to understand the elaborate experiments Mr. McDonagh had made in this research, but he would like to ask a question or two. First, was the manganese butyrate a colloidal preparation? [Mr. McDonagh: No, it was a 1 per cent. solution.] His own experience of manganese had not been so favourable as that of Mr. McDonagh. He (Dr. Gray) found that in a case of boils which responded well to manganese one could get almost miraculous results from one or two injections, and, on Mr. McDonagh's advice, he had never given more than three injections, at two or three days' interval. But he had often found that some weeks afterwards there had been a relapse, and then, at that stage, the giving of more collosol manganese produced no benefit. That occurrence did not seem to fit in with the explanation Mr. McDonagh had given. He had understood that the colloidal manganese required some peptone to keep it protected. [Mr. McDonagh: It had none.] He was interested to hear that, because he had assumed that one was not dealing with the effect of manganese at all, but with protein shock, which had a great effect on lesions of that type, but generally failed to bring the result off a second time. A further point was the following: he gathered that these metallic preparations had the effect of increasing the coagulability of the blood, while the non-metallic preparations diminished it. [Mr. McDonagh: Yes.] But he was under the impression that salvarsan and neo-salvarsan and similar preparations diminished the coagulability of the blood, and most of those who worked in this line had probably had a similar experience. [Mr. McDonagh: This is due, not to the action of the arsenic, but to the condenser action of the amino groups.]

Dr. Haldin Davis said that Mr. McDonagh had once more given the profession a remedy of considerable value in the same way as he had done when he introduced collosol manganese, which he (Dr. Haldin Davis) had himself used a good deal and with gratifying results. Indeed, he had been more fortunate with it than Dr. Gray appeared to have been. He recalled in particular two cases of sycosis in the pubic region, a region which it was notoriously difficult to treat, and which he had been able to cure by injections of collosol manganese. He had given two injections of 2 c.c. at intervals of a week, and then after waiting several weeks had given a second series. After having listened to Mr. McDonagh he was quite prepared to admit that manganese butyrate was probably a very useful remedy. But he failed to follow the reader of the paper in the arguments by which he supported his theory of the action of this drug. Mr. McDonagh had employed a terminology which was entirely his own. For example, he had used the terms "condensation" and "dispersion" to denote some electrical change in the blood and tissue fluids, but he had not indicated in any way how he measured the electrical changes thus adumbrated. He (Dr. Haldin Davis) would like further information on this point. The author had said that a change of an electrical nature had in one direction caused a quicker coagulation of citrated plasma, while a change in another direction caused a diminution of the blood-sugar. He (the speaker) was unable to follow the correlation between those

changes and the postulated electrical phenomena. His opinion was that Mr. McDonagh very likely had found a useful remedy, for which he would receive the gratitude of the members; but he thought that the discovery had really been made by the old method of trial and observation, and that its action was by no means due to electrical changes which had never been actually demonstrated to be caused by its administration.

Mr. McDonagh, in reply to the President, said that it was never suggested to use manganese butyrate in lupus vulgaris. He also said, in reply, that the clinical results from manganese butyrate were much superior to those obtained with manganese hydroxide. This was especially the case in the treatment of gonorrhœa. So far as the criticisms of his paper were concerned they could not be answered without his reiterating what he had just read. No words had been coined as suggested, and the subject-matter was extraordinarily simple, as he believed most would find it to be when reading the article at leisure. He believed he was the first to find out that arseno-benzene did not attack the syphilitic micro-organisms directly, but indirectly through the protein particles in the serum. In order to explain this indirect action he stated that his research work had led him to believe that metals acted as conductors of electricity and non-metals as condensers. Conductors caused dispersion of the protein particles, and consequently increased the area of the protective substance exposed to the parasites. One of the characteristics of dispersion was acceleration of coagulation, but the reason why the initial effect of arseno-benzene was that of retarding coagulation was because the amino groups of the benzene nucleus acted as condensers. Condensers caused the protein particles to agglutinate—an action which resulted in a loss of negative electricity—hence the reason why the first effect of prescribing salvarsan in early syphilis was to make the lesions worse. If a powerful non-metallic substance was injected into a patient with a primary sore the addition to the condensation already produced by the disease would be sufficient to bring out the rash. Simple metallic substances were required in simple infections and complex substances in protozoal infections. But it must be borne in mind that the more complex a compound became the greater was its initial condenser action. The danger of using metallic substances was that excessive dispersion led to true solution, in which state the protein particles ceased to act as protectors. This was the reason why the recurrences of syphilitic manifestations reached such a high figure when one course of injections was deemed sufficient. Also, why so many of the recurrences were of the nature of a chancre redux. He had investigated a large number of cases and was of the opinion that none were cases of reinfection. In the case of manganese butyrate in coccogenic infections clinical experience clearly showed that not more than three injections should be prescribed in any one course. If this number were exceeded the appearance of fresh lesions would be stimulated. Recurrences definitely showed that the action of treatment upon micro-organisms was indirect.

Dr. A. M. H. Gray and Dr. J. W. McNeè read a paper on *some histological and chemical observations on sclerema neonatorum.* (The paper will be published in full in a future number of this Journal.)

CURRENT LITERATURE.

INFLAMMATIONS, ETC.

GRANULOSIS RUBRA NASI. C. Ducrey. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 636.)

Two cases, aged 5 and 8 years respectively, are described occurring in the same family. The cases were typical clinically. Microscopically the skin showed slight hyperkeratosis in places, and here and there parakeratosis. Acanthosis was present with enlargement of the interpapillary projections, marked intercellular œdema (spongiosis) of Malpighian layer with vesicles here and there. The corium showed a diffuse infiltration with lymphoid cells collected here and there into groups. Some mononucleated elements were found inside the hair-follicles and sebaceous glands. There was no infiltration of the sweat-glands and the glands were not visibly altered. There was dilatation of the lymphatics, which were surrounded by an infiltration of lymphoid and plasma-cells. The author thinks the condition begins primarily as an alteration in the circulation, occurring in individuals of lymphatic diathesis often associated with chilblains and dilatation of the vessels of the extremities, probably due to some toxic agent. The hyperidrosis is a functional disturbance. He considers the alterations in the sweat-glands described by some authors as due to secondary causes. R. C. L.

POIKILODERMIA ATROPHICANS VASCULARIS (JACOBI.) J. Capelli. (*Giorn. Ital. d. Mal. Ven. e della Pelle*. 1922. fasc. ii, p. 617.)

The patient was a woman, aged 38 years. The face, neck, upper part of trunk, nates, perineum and perigenital region, upper limbs, knees, and the digital extremities of hands and feet were affected. The disease began about twenty days after parturition as a flushing of the face, and later of the other areas mentioned. This was followed by swelling of the skin. Joint and muscular pains were also present and considerable itching. On examination, the skin of the affected areas showed a whitish-red coloration, with a variegated appearance due to small red areas of dilated capillaries mixed up with areas of brownish discoloration. There was also considerable atrophy of the skin, so that the eruption looked somewhat like a radiodermatitis. The mucous membranes of lips, vulva and vagina showed atrophic lesions resembling those of lichen planus. Microscopically the skin showed atrophy of the epithelium with disappearance of the papillæ and thinning of the layers. The connective-tissue fibres of papillary and reticular layers were homogeneous, and in some areas took on the basophile stains. The elastic fibres showed a granular disintegration with fragmentation. There was definite new formation of dilated capillaries with perivascular infiltration with lymphoid cells, numerous plasma-cells and a few giant-cells. The author considers the skin condition as probably due to some endocrine-sympathetic cause, especially as it began after pregnancy and as the patient showed some signs of abnormal thyroid function. R. C. L.

A POLYMORPHIC DERMATOSIS OF LEUKÆMIC NATURE OF THE TYPE OF DUHRING'S DISEASE, ENDING IN GANGRENE OF THE SKIN. G. Mariani. (*Giorn. Ital. de Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 746.)

The patient was a male, aged 50 years. The eruption began as an erythemato-vesicular one with itching. It appeared first on the legs, and later spread to the whole body, face and arms. As the case progressed the lesions became papulo-pustular and later gangrenous. In some places the vesicular lesions were grouped in an herpetiform arrangement. The lymphatic glands were not markedly enlarged anywhere. The blood showed a slight degree of anæmia. The white blood-corpuscles numbered from 1600 to 22,000 per c.cm. There was a marked increase in the mononucleated cells. The eosinophile cells were less than 1 per cent. There were also numerous large mononucleated cells with large eccentric nucleus and abundant non-granular basophile protoplasm. Wassermann reaction was repeatedly negative. The patient died as a result of infection of and absorption from the gangrenous areas, and on post-mortem examination there was found to be a slight enlargement of lymphatic glands. The spleen was slightly enlarged and soft, the liver diffusely degenerated, bone-marrow yellow and gelantinous, and the kidneys showed a chronic degenerative nephritis. Microscopically the skin showed two kinds of change. (1) Accumulations of large mononucleated elements together with a dense infiltration of lymphocytes and plasma-cells surrounded by hypertrophied connective tissue. (2) A marked endarteritis-obliterans. The latter probably accounted for the gangrenous lesions. R. C. L.

MYELOID LEUKÆMIA OF THE SKIN. Lloyd W. Ketron and Leslie N. Gay. (*Arch. of Derm. and Syph.*, 1923, vii, p. 176.)

A case is here reported of myeloid leukæmia associated with an eruption of bluish-red nodules on the skin. The patient was a woman, aged 63 years. When first seen she was suffering from abdominal tenderness, with enlargement of the liver and spleen, and an itchy eruption of dusky red nodules along the costal margins. The blood examination at that time showed only a secondary anæmia. Within two months the nodules had spread over the entire body. A period of improvement then took place in which the liver and spleen decreased in size and the nodules gradually disappeared, leaving only discoloured macular areas. A few weeks later a recrudescence took place, skin-nodules appeared suddenly over the body and in the throat, associated with general weakness, a rise in temperature and enlargement of the liver and spleen. The blood-count then, for the first time, showed the picture of myeloid leukæmia. Death took place a month later.

Nodules taken from the skin at the necropsy showed an infiltration in the cutis, and subcutaneous tissues of myelocytes, lymphocytes, large phagocytic cells and curiously degenerated eosinophils.

This type of leukæmia cutis would appear to be rare in comparison with the lymphatic type of leukæmia. J. M. H. M.

PRURIGO IN ALEUKÆMIC LYMPHADENOMA. C. Kreibich (Prague). (*Arch. f. Derm. u. Syph.*, March, 1923, cxlii, 3, p. 396.)

The patient, a man, aged 63 years, had complained of pruritus on the shins, since November, 1919, and this had gradually become universal, sparing only the

face and scalp. Associated also was the gradual and symmetrical enlargement of the cervical, axillary and inguinal glands. The individual sizes did not exceed that of a plum, and although not adherent to surrounding parts, were not altogether unattached to each other.

It was noteworthy that itching always increased during or immediately after the glandular enlargements. The skin was covered with irritable papules of urticarial type, pigment spots and fine pitted scars, which were doubtless secondary to the scratching and rubbing admitted. The blood-count of the total white cells was 15,470; polymorpho-neutrophiles 64 per cent.; lymphocytes 25 per cent.; eosinophiles 3 per cent.; and mononuclears 9·3 per cent. Urine normal. *Nil* abnormal in heart, lungs or abdomen [presumably a normal spleen, which would exclude the disease—lymphadenoma of Hodgkin.—TRANSL.]

The treatment of the gland masses by X-rays resulted in diminution of size and relief of the itching, and the blood picture altered to—whites (total) 8780; neutrophiles 68 per cent.; lymphocytes 13 per cent.; eosinophiles 6·7 per cent.; mononuclears 9·7 per cent.

The author lays great stress on the importance of the differential diagnosis of lymphadenoma and lymphogranuloma (? Hodgkin). He states further that in his experience pruritus is a most rare symptom of lymphatic leukæmia.

H. C. S.

ON TWO CASES OF PRURIGO WITH LYMPHADENOMA. M. RAYNAUD, J. MONTPELIER, A. LACROIX. (*Ann. Derm. et Syph.*, 1923, vi serie, iv, No. 2, p. 74.)

THE authors describe in detail two male cases of lymphadenoma with prurigo, both of which died without a subsequent post-mortem examination. One patient was 44 years of age, the other 63. The cutaneous lesions were principally prurigo papules and diffuse lichenification. In both cases there were vesicles on the hands, and in one secondary pyogenic infection had taken place, chiefly on the hands, feet, face and scalp. This was probably predisposed to by the fact that he had chronic nephritis with oliguria, marked albuminuria, and a high blood urea.

Examination of the blood showed in this patient: Red corpuscles, 2,350,000; white, 94,600; polymorphonuclears, 66 per cent.; basophiles, 0; eosinophiles, 4·5 per cent.; large mononuclears, 5·5 per cent.; medium-sized mononuclears, 4 per cent.; lymphocytes, 17 per cent.; transitionals, 3 per cent.

In the other patient red corpuscles at first 6,029,000, later 4,425,000; white corpuscles at first 17,000, later 10,000. The first differential leucocyte count gave 78 per cent. polymorphonuclears and 7 per cent. eosinophiles, the second 91 per cent. of the former and 0·5 of the latter.

The Wassermann reaction was in both cases negative. There was no evidence of tubercular infection in either case. Inoculation of guinea-pigs with material from excised glands, and in one patient from pleural fluid, the intradermic tuberculin tests, and the complement-deviation test of Besredka in one case were all negative.

Detailed descriptions are given of the histological appearances of the enlarged epitrochlear glands in both cases. In one patient the prurigo was greatly ameliorated by the application of a ½ per cent. ointment of carbolic acid.

H. W. B.

URTICARIA PAPULO-PIGMENTOSA PERSTANS. L. Morini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. v, p. 967.)

After having briefly reviewed the classification of different varieties of urticaria pigmentosa as regards their clinical characters and histopathology, the author describes a case of urticaria papulo-pigmentosa perstans, which slowly developed in a patient who had previously had syphilis and malaria, but who presented no symptoms or blood changes from these infections. The characteristic histological appearances of masses of mast-cells were found. The patient showed gastric hyperacidity, eosinophilia of the blood and other signs of a chronic auto-intoxication of intestinal origin causing a condition of sympathetic hypotonus. The author thinks that this morbid syndrome explains the particular pigmentation of the lesions in urticaria papulo-pigmentosa. R. C. L.

A CONTRIBUTION TO THE STUDY OF LICHEN NITIDUS. M. Zingale. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. vi, p. 1099.)

A case of lichen nitidus (Pinkus) is reported in which the importance of a latent tuberculosis in the patient is emphasised as a causal factor. All previously recorded cases, numbering forty-six, are summarised. Of the cases fully reported some showed no history of tuberculosis, others showed its existence definitely. The author concludes that in all cases the cause is not the same, and that one can neither admit nor exclude tuberculosis as a determining factor.

R. C. L.

LICHEN NITIDUS. William B. Trimble and Edward R. Maloney. (*Arch. of Derm. and Syph.*, 1923, vii, p. 452.)

Three typical cases of this rare condition, described by Pinkus, are here reported and the histology described. The lesions were widely distributed, and consisted of minute, discrete, skin-coloured papules, which gave rise to no subjective symptoms.

Histologically the lesion presented the picture of a granuloma, and, as a positive reaction to tuberculin was obtained in several cases, it was thought that it might be due to a tuberculin toxin. Treatment had little effect on the condition, but the lesions tended to disappear spontaneously, possibly owing to the fact that the individual had acquired an immunity to the toxin.

J. M. H. M.

BAKERS' DERMATITIS. Oscar de Jong. (*Brit. Med. Journ.*, 1923, p. 65.)

A note read before the Liverpool Medical Institution, in which the author points out that the lesion occurs in men mixing the ingredients by hand. It does not appear among those men who prepare the yeast or handle the dry flour. He presumes that the 3·6 per cent. salt solution added to the flour is the real causative factor, the temperature of the bakehouse resulting in the crystallisation of the salt on the arms of the workman, the crystals then being rubbed into the skin during kneading. M. S. T.

HYDROA VACCINIFORME SEU ÆSTIVALE. Francis Eugene Senear and Harry W. Fink. (*Arch. of Derm. and Syph.*, 1923, vii, p. 145.)

Ehrmann showed that typical lesions, with scar-formation, could be experimentally produced on the covered parts of the body by Finsen light with a blue

filter. In hydroa vacciniforme the lesions appear some hours after exposure to the sun's rays, while from heat rays the reaction is immediate. Changes in temperature and wind are excitants also, but to a minor degree.

Hæmatoporphyrin occurs in the urine in diseases of the liver in connection with tuberculosis, etc. Urine containing it may be only slightly coloured, or of deep red. When introduced in the body it causes photo-sensitisation. In patients suffering with hydroa vacciniforme the hæmatoporphyrin occurs during the attacks.

Linser was able to produce hæmatoporphyrinuria in a patient suffering from hydroa vacciniforme by exposing the hand to a quartz lamp.

Several cases have been described in tuberculous people. J. M. H. M.

PITYRIASIS RUBRA PILARIS—FAMILIAL TYPE. Erwin P. Zeisler. (*Arch. of Derm. and Syph.*, 1923, vii, p. 195.)

Four cases are here described in a father and three children. These cases were of a mild type, presenting atypical features resembling psoriasis, but differing from the latter disease in the presence of definite acuminate papules and the absence of bleeding points on removal of the scales.

These cases showed a marked improvement with thyroid therapy internally, and the free use of baths, followed by a mild emollient, such as benzoated lard or lanoline. J. M. H. M.

ANIMAL AND VEGETABLE PARASITES.

ON THE CONTINUANCE OF THE EPIDEMIC OF GRAIN ITCH IN THE PROVINCE AND CITY OF BOLOGNA AND A CIRCUMSCRIBED EPIDEMIC IN THE PRISONS OF THE SAME CITY. D. Majocchi. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 124.)

The cases showed the usual erythemato-papular and papulo-vesicular lesions, sometimes complicated with urticarial and suppurative lesions. The epidemic began in the city, and in the month of June, 1921, 140 persons were affected—10 in the city, 125 in the prison in the city, and 5 in the country round about. In July 10 more cases occurred, in August 18, in September 37, and in October 80 cases. The large number of cases at this time of year was attributed to the amount of grain which was being handled and distributed both in the city and country districts. The infection was spread not only by grain, but by sacks which had contained grain and by infected straw used for beds.

R. C. L.

FIRST AND RAPID APPEARANCE OF GRAIN-ITCH IN THE COMMUNE OF UDINE. G. Murero. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 127.)

This article describes a very similar epidemic of grain-itch to the previous one. It also occurred in the summer and autumn months. There is also a very good full-page illustration of the eruption. R. C. L.

CULTURES OF TRICHOPHYTON GYPSEUM FROM THE CIRCULATING BLOOD IN TRICHOPHYTOSIS PROFUNDA WITH LICHEN TRICHOPHYTICUS. G. A. Ambrosoli. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1921, fasc. iii, p. 233.)

Ambrosoli describes a case of kerion ringworm in a child, aged 11 years. From the hairs the trichophyton gypseum asteroides was cultivated. A lichenoid rash also appeared on the thorax, abdomen, and upper part of arms, together with an enlargement of the inguinal and cervical glands. On two successive days whilst the general rash was at its height blood cultures were taken, and on the second occasion a pure culture of the trichophyton gypseum asteroides the same as from the kerion lesions was obtained. This proves that the trichophytides are due to the actual presence of fungus elements in the circulation, and supports the contention that the trichophytide in ringworm is analogous to the tuberculide in tuberculosis. R. C. L.

INTERDIGITAL ENDOMYCETIC DERMATITIS. C. Lombardo. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 674.)

The patient, a young woman, aged 19 years, showed a dermatitis between the ring and middle fingers of each hand of four years' duration. The area was reddened and covered with sodden, macerated skin. Microscopically abundant mycelium mixed with levuliform elements was found. White cultures were obtained on Sabouraud's and other media. Blood-cultures, complement deviation and agglutination tests with the fungus were negative. The fungus corresponded to a form of *Endomycetes albicans* described previously by Kaufmann and Fabry. The best results in treatment were obtained with a 5 per cent. chrysarobin ointment. Photographs of the lesions and of the fungus and a list of previously published cases are given. R. C. L.

A NEW MYCETES (HAPLOGRAPHIUM OF DE BELLA AND MARENGO) AND THE SKIN-LESIONS PRODUCED BY IT. A. de Bella and G. Marengo. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 690.)

The patient was a man, aged 30 years, who showed an isolated lesion on right cheek. The lesion was triangular in shape, deep red in colour and raised above the surface, ulcerated at the lower part and discharging blood-stained viscous pus. The edges felt hard and the whole lesion resembled a gumma. The cutaneous tuberculin test and Wassermann reaction were both negative. Microscopically the lesion showed a granuloma with giant-cells, epithelioid, plasma-cells and many polymorphonuclear leucocytes. Many mast-cells were also present. Spores were also found, but mycelium was not demonstrated in the sections. Cultures were made on Sabouraud's proof medium and incubated at about 20°. The cultures were greyish-green in colour, with a polycyclic edge, and mammilated on the surface. Later they became more depressed in the centre and had a cerebriform appearance, and old cultures (2–3 months) became almost black. The cultures consisted of mycelium and roundish and oval spores. This fungus was successfully inoculated on a rabbit's skin, producing a lumpy lesion, which broke down and suppurated, and from which the same fungus was again obtained in culture. The authors propose the name "haplo-

graphium" (de Bella-Marengo) for the fungus and "haplographiosis cutanea" for the skin-lesion. R. C. L.

CUTANEOUS MYCOSIS DUE TO HEMISPORA STELLATA. R. Porcelli. (*Giorn. Ital. de Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 698.)

This is the first case of hemisporosis recorded in Italy. After giving a short history of previously reported cases elsewhere the author describes his case. The patient was a girl, aged 19 years. The primary infection took place over the external malleolus of left leg, and rapidly spread by the lymphatics up the limb, producing nodulo-gummatous lesions, which ulcerated and formed scrofulous-like sores. These had a tendency to partial healing. The lesions healed rapidly under treatment with iodides, but recurred repeatedly with fresh gummatous lesions. The Wassermann reaction, tuberculin skin test, and inoculation of guinea-pigs were all negative. The intra-dermic reaction, agglutination and complement-fixation tests to *Sporotrichium B* were all positive. Microscopically the lesion showed a granuloma with giant-cells, epithelioid cells with small round-cells and polymorphonuclear leucocytes. There was also an endo-,meso- and peri-arteritis of the blood-vessels. No fungus elements were visible in the sections. A typical culture of *Hemispora stellata* was obtained. Gougerot, who saw the cultures, concurred in the diagnosis. Inoculations of rabbits were successful on subcutaneous, intramuscular and intraperitoneal injection, with the formation of gummatous nodules, which broke down and histologically were identical with the lesions in the patient. Good photographs are given of the clinical lesion, of the cultures, microscopic appearance of fungus and inoculation lesions in the rabbit. R. C. L.

A CONTRIBUTION TO THE HISTO-PATHOLOGICAL STUDY OF PITYRIASIS VERSICOLOR. P. A. Meineri. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. iii, p. 755.)

The author found that the skin in pityriasis versicolor showed an increased thickening of the horny layer, which is very loosely attached to the stratum lucidum. Areas of parakeratosis were also seen. The *Microsporon furfur* lives exclusively in the horny layer and chiefly in the internal and middle part of it. The basal part is rarely invaded, and if so only by the terminal parts of the mycelium. In the Malpighian layer there is intra- and intercellular œdema, slight infiltration of lymphocytes, and in the upper layers may show microscopic vesicles. The basal cells sometimes show an increase of pigment. In the corium there is dilatation of the blood-vessels, numerous proliferated connective-tissue cells, a few lymphocytes round the vessels, and occasionally plasma-cells. There are also pigment-granules arranged in small groups. Four microphotographs of the skin-lesions are shown. R. C. L.

ON A DERMATOSIS OF ULCERATIVE TYPE OF PROBABLE PENICILLARY ORIGIN. M. Rebaudi and G. B. Podestà. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. iv, p. 871.)

The patient was a girl, aged 14 years, with ulcerated lesions on the legs towards its lower third. The ulcers had infiltrated festooned edges. Microscopically the infiltrate consisted chiefly of lymphoid cells, a few plasma-cells and leucocytes and a very few eosinophile cells. Giant-cells were completely

absent. From the lesions a culture of *Penicillium glaucum* was obtained. An intradermic cutaneous reaction was obtained to a filtrate of the fungus growth. Complement-fixation tests with an aqueous solution of the cultural material were positive, and negative with actinomycotic antigen. Inoculated into a guinea-pig slowly developing nodular lesions from which the penicillium was obtained developed. From the above facts the authors think that the *Penicillium glaucum* was the probable cause of the skin lesions. R. C. L.

THE TREATMENT OF PARASITIC INFECTIONS OF THE BEARD WITH ENDOVENOUS INJECTIONS OF IODINE SOLUTION. F. Ronchese. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. iv, p. 918.)

Injections of Gram's solution of iodine were given after sterilisation and dilution with two parts of distilled water. Injections were given at daily, two-day or five-day intervals. Five cases of tinea barbæ were so treated, with very good results in three of them. R. C. L.

SPOROTRICHOSIS. Earl D. Crutchfield. (*Arch. of Derm. and Syph.*, 1923, vii, p. 226.)

Two typical cases are here recorded in which the organisms were demonstrated in smears and in sections of nodules. Both cases responded to potassium iodide internally, but it took about 2½ months to effect the cure. J. M. H. M.

NEW GROWTHS.

A CASE OF CARCINOMA OF THE SKIN ARISING FROM THE SUDORIFEROUS TUBULES. L. Morini and P. Montagnani. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1921, fasc. vi, p. 733.)

The authors describe a case of carcinoma starting on the heel of the left foot, and spreading rapidly by the lymphatics. Microscopic examination of the case showed that the lesion had begun in the superficial dermis. It had the general appearance of a basal-celled carcinoma, with the cells arranged after the manner of the sudoriferous tubules. Epithelial pearls were absent. The most typical parts were seen at the periphery, the cells in the central parts showing considerable degeneration. Metastases occurred exclusively by the lymphatics and occurred very rapidly. Illustrations of the glandular infection in left groin and six microphotographs of the sections of the lesion are given. R. C. L.

PRELIMINARY NOTE ON THE PROBABLE DESTRUCTIVE ACTION OF POTASSIUM PERMANGANATE ON CONDYLOMATA ACUMINATA OF THE URETHRA. Augusto Oro. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. i, p. 55.)

A case of condylomata acuminata of the fossa navicularis of the urethra was treated with daily lavage with a solution of potassium permanganate (1 in 4000). Twenty irrigations were sufficient to cause the lesions to disappear entirely. The author recommends the method as worthy of trial in such cases.

R. C. L.

A CASE OF CUTANEOUS CYLINDROMA. D. Majocchi. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 122.)

The case here recorded showed a small tumour in the skin of the right eyebrow in a man, aged 28 years. It had a yellowish appearance, somewhat like xanthoma, but on excision proved to be a cylindroma consisting of cylindrical masses, some isolated, others anastomosing with each other. These masses consisted of flat, rounded oval or slightly fusiform cells lying close to one another. Round each mass of cells was a fairly well-marked connective-tissue layer. There was no evidence that the tumour had grown from the skin over it, or from the glands or follicles in the neighbourhood. The author was of opinion that it had developed from endothelium of blood and lymphatic vessels, but could not exclude its perithelial origin. R. C. L.

THE PRECANCEROUS DERMATOSIS OF BOWEN. L. Martinotti. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 182.)

Two cases of this condition are fully reported, one with a single lesion over the sternum, the other with three lesions—one over sternum, another on left breast, and another in right groin. They showed a papillomatous and crusted surface, and resisted all local treatment till their epitheliomatous nature was demonstrated by biopsy. Photographs of the skin lesions and six drawings of the microscopic appearances are shown. The analogy between this condition and Paget's disease of the nipple and Darier's disease is fully discussed R. C. L.

A PECULIAR CASE OF MOLLUSCUM CONTAGIOSUM GIGANTICUM ON THE SCALP OF AN INFANT. M Quattrini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. v, p. 1003.)

This case was peculiar in that the lesion appeared on the scalp of an infant, aged 3 months. The lesion was a solitary large one with no umbilication, and on excision found to show the typical microscopic appearances of molluscum contagosium. Taking into consideration the usual incubation period of nine weeks to six months for molluscum lesions, the appearance of a lesion in such a young child is peculiar. R. C. L.

NEW RESEARCHES ON MOLLUSCUM CONTAGIOSUM. C. Gargano. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. vi, p. 1141.)

As a result of a perusal of the literature on the subject and the author's own experiments, he concludes that molluscum contagiosium runs a clinical course like an infectious disease, even although the experiments of positive inoculation are very doubtful and not at all convincing. The molluscum bodies, whilst resembling those seen in molluscum contagiosum of amphibians and contagious epithelioma of fowls, differ in many important characters, both morphologically and chemically. The initial lesion in the Malpighian layer might possibly in some cases arise from the epithelium of the hair-follicles or sebaceous gland. In the present state of our knowledge it is not possible to affirm that the corpuscles of Benda and the numerous chromatophile endo- and extra-cellular granules are parasites. If one allows that the molluscum contagiosum lesion is surrounded by a connective-tissue membrane it should be considered as a neoplasm. Against this, however, is the evolution of the lesion, which may heal either spontaneously or by the rubbing of the clothes on it. R. C. L.

PRIMARY GENERALISED SARCOMATOSIS OF THE SKIN. A. Crosti. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. vi, p. 1113.)

Two cases are described. One case showed the classical picture of such neoplasms both in its symptomatology and course. The other was in a man, aged 37 years, who developed multiple indolent nodules on the legs. Many of the lesions resembled tertiary syphilitic ones. The Wassermann reaction was negative. Antisyphilitic treatment caused a complete disappearance of the lesions, but about a month later they reappeared, and on excision were found to show the typical structure of a small round-celled sarcoma. Later metastases occurred in the testicle and diffusely over the skin. R. C. L.

A CASE OF ACANTHOSIS NIGRICANS. E. Bruusgaard. (*Forh. i Medicinsk Selskab.*, 1922, p. 59.)

A case of acanthosis nigricans is reported in a woman, aged 65 years, who had been admitted into hospital on account of a generalised pruritus of one year's duration. The typical skin changes were most marked in the axillæ and genitocrural folds, on the epigastrium, loins and external genitalia. The buccal mucosa was free. In addition there were numerous pigmented nævi on the back, and a tumour (size of hen's egg) in the right axilla proved to be an adenoma of the sweat-glands. An exploratory laparotomy revealed carcinoma ventriculi, with a secondary tumour in the liver, and gland metastases in the lesser omentum. Attention is drawn to the not infrequent association of pruritus with malignant disease. W. J. O.

TREATMENT.

THE TREATMENT WITH X-RAYS AND RADIUM OF RHINOPHARYNGOSCLEROMA. L. Mazzoni. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 736.)

Fifteen cases of rhinoscleroma affecting the nose, pharynx and larynx were treated with X-rays and radium. The author concludes that of all forms of treatment, including the knife, Volkmann's spoon, thermocautery and caustics, the best results are obtained with radium. R. C. L.

THE TREATMENT WITH RADIUM OF SOME FORMS OF LOCALISED CIRCUMSCRIBED HYPERKERATOSIS OF THE SOLES OF FEET. V. Palumbo. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii, p. 738.)

The author recommends radium in the treatment of all forms of localised hyperkeratoses of the soles such as callus and clavus. Sometimes one, and at most two, applications are sufficient to cure each case. The dose administered is not mentioned. R. C. L.

THE X-RAY TREATMENT OF RINGWORM. C. Guarini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. vi, p. 1182.)

The author states that all accidents from X-raying scalps for ringworm can be avoided by the use of filters and by exact technique. He uses the Kienbock-Adamsom method. He places the tube at 25 cm. from the scalp and uses a

filter of 2 mm. of aluminium. He prefers the Coolidge tube with a spark-gap of 20–25 cm., with a current of 2–3 milliampères. By this method, after treating over one hundred cases, he obtained in all cases complete epilation in 15–20 days, and in no case was there any partial or complete permanent alopecia.

R. C. L.

ASPECIFIC PROTEIN THERAPY IN THE TREATMENT OF SKIN AND VENEREAL DISEASES. G. Mariani. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. ii. p. 739.)

One hundred and fifty cases were treated, composed of 43 skin cases (28 dermatoses of various type and 15 of pyodermias), 76 of gonorrhœa, most of which had complications, and 31 of adenitis associated with venereal ulcers or other infected lesions. Comparisons were made on the action of specific hetero-sera and hetero-vaccines, of auto-sera, auto-plasma and auto-hæmic injections; also with a specific hetero-sera and hetero-vaccines; with protein substances of various kinds, including milk, peptone, nuclein and various colloid metals.

In dermatoses of an infective nature (especially pyodermia) much more constant results were obtained with specific than with aspecific methods. Autogenous vaccines always gave good results, whilst for the most part hetero-sera, milk and peptone failed to do good. These latter methods were also inefficacious in dermatoses of unknown origin, such as eczemas and psoriasis. In the cases of pemphigus and dermatitis herpetiformis, however, good results were obtained by injections of the patient's own serum, plasma, or blood. In such cases hetero-sera vaccines and hetero-proteins failed to give any result. In venereal ulcers hetero-proteins gave better results than auto- or hetero-sera and vaccines. Of the hetero-proteins tried, peptone gave the best results.

The author's experience in using protein therapy was that the temperature reaction varied very much in different cases even when using the same product. If injections were given during fever sometimes it caused a fall of temperature by crisis, in other cases it caused an increase of temperature, but large quantities of protein were often injected without producing any temperature. Generally speaking the temperature after the introduction of sera and vaccines rose more slowly and gradually than after the use of hetero-proteins, which produced more sudden rises associated with rigors. No connection was observed between the temperature reaction and the therapeutic result. Headache was a frequent symptom sometimes associated with a rise of temperature, at other times quite independently. Nausea, vomiting, vertigo, and a feeling of general prostration were sometimes observed. Enlargement of the spleen was noticed in acute reactions after hetero-protein and especially in those who had previously had malaria. Albuminuria, usually transitory, without casts in the urine, was found in a few cases after the use of hetero-proteins; marked sweating was also seen apart from any falling temperature. The blood-pressure fell in some cases, especially after intravenous injections of peptone. Intramuscular injection of peptone did not produce this fall of pressure. The blood picture varied considerably in different cases after injections. This was particularly so in cases with a rise of temperature. Frequently an eosinophilia occurred, but not constantly, and also a polynuclear leucocytosis the first time and a lymphocytosis a second time. In the cases which showed a polynuclear leucocytosis and eosinophilia the therapeutic result was usually good. In some cases focal reactions resulted after the

injections, sometimes limited to the lesions, at other times extra-focally and leading to an extension of the disease. The focal reactions were usually followed by an improvement in the lesion, and any spread of the disease was generally of a benign nature. There was no constant relation between focal reactions and therapeutic results. In the itching of eczema and dermatitis herpetiformis, injections, specially of auto-serum, proved beneficial. Allergic reactions were variable; symptoms after the first injection were sometimes seen with hetero-sera, peptone, hetero- and auto-vaccines, but rarely with milk. Anaphylactic reactions, 8 to 12 days after the beginning of the treatment, were fairly frequent after the use of hetero-sera, occasional after milk, rare after peptone and hetero-vaccines, and never after autogenous vaccines.

Interesting reactions sometimes followed the injection of two different substances. Anaphylactoid reactions occurred with milk after hetero-serum, with peptone after milk and so on. In one case a marked anaphylactic reaction occurred with an injection of egg-albumin given some hours after a peptone injection.

To sum up, aspecific protein-therapy was found to be of very little use in dermatoses of unknown cause which are probably not infective, although the symptoms might be somewhat ameliorated. In pyogenic dermatoses hetero-protein therapy has very little effect but specific autogenous vaccines were undoubtedly advantageous. The adenitis of venereal ulcers were almost constantly favourably influenced, especially if in the early stages, and venereal ulcers, although improved after the injections, always required local treatment as well. R. C. L.

SYPHILIS, ETC.

ASPECIFIC PROTEIN-THERAPY IN CERTAIN MANIFESTATIONS OF SYPHILIS. C. Barile. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1923, fasc. i. p. 61.)

The author recommends the use of aspecific protein therapy (milk, casein, peptone, etc.) in addition to the ordinary antispecific remedies. He quotes no cases, but simply suggests the method as one which should be tried.

R. C. L.

WASSERMANN AND FLOCCULATION TESTS COMPARED IN 1000 CASES. A. L. Urquhart. (*Lancet*, January 20th, 1923, p. 125.)

The conclusions reached are that the flocculation test gives as reliable results as the Wassermann reaction and is preferable on account of its greater simplicity. Details of the technique used in both tests are given, and in 1000 cases there is a lack of agreement in only 2 per cent. of the cases.

The sera tested were taken from syphilis treated and untreated, from suspected syphilis cases and from cases of disease other than syphilis.

In cases of untreated syphilis weak positive flocculation tests corresponded to weak positive Wassermann reactions and strongly positive ones to strongly positive, but in treated cases this correspondence no longer held, the F.R. test always being rather stronger than the W.R., which would suggest that the F.R.

does not disappear from the sera in cases of syphilis infection so rapidly as the W.R.

Disadvantages of the F.R. are that readings are taken after 24 and 48 hours' incubation, which unduly delays the results as compared with the W.R., and that unless the sera remain sterile a false appearance of flocculation occurs owing to the growth of organisms during the long incubation at 37°.

J. A. D.

ARSENIC CONTENT OF BLOOD AND URINE AFTER INTRAVENOUS INJECTION OF VARIOUS SALVARSAN PREPARATIONS, AND ITS RELATIONSHIP TO DAMAGE BY ARSENIC. Wechselmann, Lockemann and Ulrich. (*Arch. f. Derm. u. Syph.*, 1923, cxlii, 2, p. 163.)

A most laborious and painstaking investigation, with tabular results on 68 blood and 63 urine contents of arsenic in 57 individuals, extending over a period of 2 years, resulted in the following conclusions:

The respective amounts of arsenic depend—

(1) On the chemical nature of the injection used, *i. e.* sodium salvarsan and neo-silver-salvarsan are excreted much more rapidly from the blood than neosalvarsan, sulfoxylate and silver-salvarsan.

(2) On the retentive and excretory idiosyncrasies of the organism itself. Retention in the blood of large quantities of arsenic need not necessarily be followed immediately by clinical manifestations. It would seem that the excretory potentialities are subject to somewhat rapid variation in the same subject, during a course of treatment, and that much delay in this respect increases the danger of damage.

The authors were not able to determine whether arsenic found chemically in the organs can re-enter the circulation.

They do not believe, moreover, on clinical grounds that arsenic retained in combination with tissue proteins is capable of therapeutic effects at some future date.

H. C. S.

MERCURIAL DERMATOSES. Johan Almkvist. (*Acta Dermato-venereologica*, 1922, iii, 1–2, p. 106.)

This long, interesting paper with much commentary is based on the examination of thirty-eight cases with two deaths. This appellation is chosen in preference to others in the literature to include the large variety of skin lesions which may occur, though the designation of exanthemata is approved. Two main groups are made: (*a*) Simple mercurial dermatosis or exanthem, due to the action of mercury alone; (*b*) complicated ditto, in which some additional ætiological factor is concerned. In cases of the second group the continuation of the skin condition, after elimination of the mercury, is due to bacterial infection, the nature of which determines the severity of each case. In this series the most frequent site of the *first* appearance of the skin lesions was the peripheral parts of the limbs. The apparent predisposition of these cyanosed areas is contrasted with their freedom from early syphilitic rashes. The involvement of the buccal, laryngeal and intestinal mucous membranes denoted simply an expansion of the cutaneous lesions. The histopathology is described (accom-

panied by several coloured plates) to show four stages in the alteration of the skin: (1) Vascular dilatation with some slight œdema; (2) increase of the œdema and the appearance of increased endothelial cells and a perivascular cellular infiltration consisting of plasma-cells, mast-cells and eosinophilic cells; (3) development of bacteria from the surface with their penetration into the epidermis and the formation of pseudo-abscesses about the sebaceous follicles; (4) pus formation. The initial changes are like those occurring in other organs, the later stages being peculiar owing to secondary infection from the skin surface.

The pathogenesis of those conditions lies probably in the idiosyncrasy towards mercury of certain sympathetic ganglionic cells governing a particular organ. A lengthy bibliography completes this paper, which does not lend itself to proper abstraction. W. J. O.

A STUDY OF EROSIVE AND GANGRENOUS BALANITIS. Julius Brams and Isadore Pilot. (*Arch. of Derm. and Syph.*, 1923, vii, p. 429.)

In this paper a series of cases of gangrenous and erosive balanitis are reported. In them the history of sexual exposure was remote or absent, so that they were apparently non-venereal in origin. A common characteristic of the cases was the presence of long phimotic foreskins. In the purulent secretions, fusiform bacilli, spirochætes and staphylococci were constantly found.

According to the writers, balanitis may result from organisms normally present as saprophytes, under suitable local conditions associated with diminished general resistance. Early recognition and treatment of the disease is imperative, as the process spreads with great rapidity.

J. M. H. M.

THE THERAPEUTIC ACTION OF BISMUTH IN SYPHILIS. C. Levaditi (from the Institut Pasteur, Paris). (*Lancet*, March 31st, 1923, p. 639.)

The paper consists largely of an analysis of reports from various sources on the value of bismuth in syphilis. The forms of bismuth chiefly used are the basic tartro-bismuthates of potassium and sodium (trépol), and the 95 per cent. suspension of metallic bismuth in a sterile iso-tonic solution (neo-trépol).

Practically all are in agreement as to the improvement which occurs both in early and late cases and in neuro-syphilis. The results on the Wassermann reactions are less definite, there is evidence that it is favourably affected, but it would appear that it is too early as yet to reach a definite conclusion.

Bismuth seems to have a special use in those cases which do not react favourably to or have become resistant to arsenic and mercury. The most frequent complication, *i.e.* the "bismuth line" on the gums and stomatitis, is more common in those who take no care of their teeth, and is said to be more favourable than the mercurial form. It is stated that when neo-trépol is used buccal symptoms are very rare. J. A. D.

QUARTERLY SURVEY OF DERMATOLOGICAL LITERATURE.

ERYTHEMAS, INFLAMMATIONS, ETC.

Alopecia, Endocrino-Sympathetic Origin of. L. Franckel et Juster. (*Bull. de Soc. Franç. de Derm. et de Syph.*, March, 1923, No. 2, p. 113.)

Alopecia and Poliosis of the Eyelids. W. C. Posey. (*Journ. Amer. Med. Assoc.*, April 28th, 1923, lxxx, No. 17, p. 1204.)

Amyloid Disease of the Skin, Recognition of. C. Gutmann. (*Derm. Zeitschr.*, April, 1923, p. 65.)

Bullous Eruptions in Hæmorrhagic Sarcomas of Kaposi and in Lichen Planus. F. Wise and J. J. Eller. (*Arch. of Derm. and Syph.*, May, 1923, vii, No. 5, p. 625.)

Bullous Impetigo Contagiosa, Institutional Epidemics. F. C. Knowles and H. G. Munson. (*Arch. of Derm. and Syph.*, March, 1923, vii, No. 3, p. 376.)

Callous Ulcers of the Leg, The Treatment of. H. Hecht. (*Derm. Zeitschr.*, January, 1923, p. 313.)

Congenital Cutaneous Abnormality, Rare Case of (Cutis Marmorata Teleangiectatica Congenita). Cato H. J. van Lohnizen. (*Acta Dermato-venereologica*, iii, 1–2, p. 202.)

Cutaneous Tests, Histopathology of. A. Strickler. (*Arch. of Derm. and Syph.*, March, 1923, vii, No. 3, p. 379.)

Dermatomyositis. H. Joachim. (*Arch. of Derm. and Syph.*, March, 1923, vii, No. 3, p. 326.)

Dermatoses of Monkeys and in Apes. F. D. Weidman. (*Arch. of Derm. and Syph.*, March, 1923, vii, No. 3, p. 289.)

Dermatosis Dymenorrhoica Symmetrica, A Distinct Disease-Type. R. Poliand. (*Derm. Zeitschr.*, April, 1923, p. 89.)

Dermatitis Venenata due to Coloured Paper. H. G. Rowell. (*Arch. of Derm. andSyph.*, May, 1923, vii, No. 5, p. 603.)

Diseases of Ectodermal Origin. J. Henrichs and P. Henriksen. (*Norsk. Mag. f. Lægev.*, January, 1923, p. 1.)

Eczema, Infantile, Dietary Considerations. J. R. Gerstley. (*Journ. Amer. Med. Assoc.*, April 21st, 1923, lxxx, No. 11, p. 1141.)

Erythemata, Variations of Vago-Sympathetic Equilibrium in. M. Laurent. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, March, 1923, p. 134.)

Granuloma Inguinale. I. M. Gage. (*Arch. of Derm. and Syph.*, March, 1923, vii, No. 3, p. 303.)

Granuloma Inguinale in Boston. G. C. Shattuck. (*Boston Med. and Surg. Journ.*, April 12th, 1923, clxxxviii, No. 15, p. 530.)

Granuloma Pediculatum. F. Falkenstein. (*Derm. Zeitschr.*, January, 1923, p. 299.)

Hydroa Vacciniforme. F. E. Senear and H. W. Fink. (*Arch. of Derm. and Syph.*, February, 1923, vii, No. 2, p. 145.)

Hydrogen-Ion Concentration on Surface of Healthy Skin. H. Sharlitt and M. Scheer. (*Arch. of Derm. and Syph.*, May, 1923, vii, No. 5, p. 592.)

Hyperkeratosis of Thenar Eminence with Obstetrical Palsy, Case of. Lortat-Jacob. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, March, 1923, No. 3, p. 157.)

Keratodermia of Palm following Brachial Plexus Lesion. L. Franckel. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, March, 1923, No. 2, p. 117.)

Keratodermia Blennorrhagica. H. L. Kretschmer. (*Journ. Amer. Med. Assoc.*, April 7th, 1923, lxxx, No. 14, p. 993.)

Leishmaniasis with Subcutaneous Gumma. (Micro-photos.) P. Vigne and E. Pringault. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, February, 1923, No. 2, p. 99.)

Leprosy, Different Forms of, especially Lepra Tuberculoides. H. P. Lie. (*Medicinsk Revue*, January–February, 1923, p. 143.)

Leucoderma Acquisitum Centrifugum. J. H. Stokes. (*Arch. of Derm. and Syph.*, May, 1923, vii, No. 5, p. 610.)

Leuconychia, Acute Generalised, in a Man of 22. (Illustrated.) B. Ballet. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, February, 1923, No. 2, p. 77.)

Lichenification of the Genito-crural Fold. (Illustrated.) C. M. Pautrier. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, March, 1923, No. 3 [R.S.], p. 7.)

Lupus Erythematosus and Systemic Disease. W. H. Goeckeman. (*Journ. Amer. Med. Assoc.*, February 24th, 1923, lxxx, No. 8, p. 542.)

Mammary Eczema and Amenorrhœa, Case of. Lortat-Jacob. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, March, 1923, No. 3, p. 133.)

Myeloid Leukæmia of the Skin. L. W. Ketron. (*Arch. of Derm. and Syph.*, February, 1923, vii, No. 2, p. 176.)

Oriental Sore in the United States. R. A. Lambert. (*Journ. Amer. Med. Assoc.*, April 7th, 1923, lxxx, No. 14, p. 986.)

Pellagra, Ætiology of. J. W. Jobling. (*Journ. Amer. Med. Assoc.*, February 10th, 1923, lxxx, No. 6, p. 365.)

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Pituitary Gland Dystrophies, Skin-changes in. L. Hollander. (*Arch. of Derm. and Syph.*, May, 1923, vii, No. 5, p. 634.)

Pityriasis Rosea. W. J. Highman. (*Arch. of Derm. and Syph.*, February, 1923, vii, No. 2, p. 163.)

Pityriasis Rubra Pilaris, Familial Type. E. P. Zeisler. (*Arch. of Derm. and Syph.*, February, 1923, vii, No. 2, p. 195.)

Pruritus Ani, Ætiology and Pathogenesis. J. F. Montague. (*New York Med. Journ.*, April 18th, 1923, cxvii, No. 8, p. 469.)

Psoriasis, Syphilis, Congenital and Acquired, in. Leredde. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, March, 1923, No. 3, p. 138.)

Purpuric Eruption, Chronic Case without Blood Changes. J. H. Arnett and F. D. Weidman. (*Journ. Amer. Med. Assoc.*, April 21st, 1923, lxxx, No. 16, p. 1132.)

Raynaud's Syndrome in a Non-syphilitic Infant, with a Remarkable Family History. F. Parkes Weber. (*Brit. Journ. Child. Dis.*, January–March, 1923, xx, p. 25.)

Sclerodermia, Mutilating, Progressive, Case of. (With photos.) RONDINESCO. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, March, 1923, No. 3, p. 151.)

Tuberculides of the Face, Papulo-necrotic and Nodular. LOUSTE. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, March, 1923, No. 3, p. 120.)

Tylosis, Hereditary. J. D. ROLLESTON. (*Brit. Journ. Child. Dis.*, January–March, 1923, xx, p. 16.)

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Urticaria Pigmentosa in a Man of 52. C. SEMON and J. BRALEY. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, February, 1923, No. 2, p. 66.)

Vitiligo, Scleroderma and Congenital Anomalies. A. LERI. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, March, 1923, No. 3, p. 127.)

PARASITES.

Aspergillus in Scalp Lesions after Red-bug Bites. K. M. LYNCH. (*Arch. of Derm. and Syph.*, May, 1923, vii, No. 5, p. 599.)

Centipede-bite and Scorpion-sting, with Regard to War Experience in Macedonia. H. MAYER. (*Derm. Zeitschr.*, February, 1923, p. 1.)

Disseminated Ringworm of Animal Origin. (Illustrated.) JEANSELME. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, February, 1923, No. 2, p. 82.)

Microsporon Audouinii, Further Contributions. L. ARZT and H. FUHS. (*Acta Dermato-venereal ogica*, iii, 1–2, p. 1.)

Nail Disease due to Trichophyton Endothrix Violaceum. J. HELLER. (*Derm. Zeitschr.*, February, 1923, p. 13.)

Sporotrichosis, Cases of. E. D. CRUTCHFIELD. (*Arch. of Derm. and Syph.*, February, 1923, vii, No. 2, p. 226.)

NEW GROWTHS.

Acanthoma of the Mucous Membranes of the Lips, with Notes on the so-called "Papillomatoses Cutis" (Vollmer, Fautl). ARTHUR ALEXANDER. (*Acta Dermato-venereal ogica*, iii, 1–2, p. 52.)

Arsenic Cancer, with Remarks on other Cutaneous Manifestations due to Arsenic. A. L. FÖUSS. (*Derm. Zeitschr.*, January, 1923, p. 257.)

Arsenic Carcinoma, with Notes on Other Effects of Arsenic upon the Skin. AAGE L. FÖUSS. (*Derm. Zeitschr.*, Bd. xxxvii, Heft 5–6, p. 257.)

Calcification of the Skin. R. R. DUCASSE. (*Arch. of Derm. and Syph.*, March, 1923, vii, No. 3, p. 373.)

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Epithelioma developed upon Keloid. J. BELOT and L. NAHAN. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, February, 1923, No. 2.)

Paraffin-oil Tumours in Monkeys, Experimental. F. D. WEIDMAN. (*Arch. of Derm. and Syph.*, February, 1923, vii, No. 2, p. 209.)

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Tumour after Injection of Mercury Salicylate in Vegetable Oil. I. C. SUTTON. (*Arch. of Derm. and Syph.*, February, 1923, vii, No. 2, p. 223.)

Urticaria provoked by Injections of Bismuth. LÉPINAY. (*Bull. de la Soc. Franç. de Derm. et de Syph.*, March, 1923, No. 3, p. 150.)

REVIEW.

DIE LUMBALPUNKTION.*

IN this small book the author deals briefly with the anatomy and physiology of the cerebro-spinal fluid circulation, with the chemistry, cytology and serology of the fluid under normal conditions, and then discusses these aspects of the question more fully in connection with various pathological conditions. Although the book is approximately of the same bulk as Eskuchen's well-known monograph on the subject, the author has not succeeded in compressing the same amount of information into his pages, and we do not believe that the appearance of this volume is likely to endanger the popularity of Eskuchen's, or replace it as a laboratory manual. The introductory chapter deals most inadequately with recent work on the channels of absorption of the cerebro-spinal fluid. Further, in the final chapter dealing with the diagnostic value of certain variations in the composition of the fluid, the information given is extremely scrappy. Finally, technical details of the various reactions are inadequate if the book is intended as a laboratory manual. However, Pappenheim gives a very readable general account of the subject, and there are no notable gaps.

F. M. R. W.

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* *Die Lumbalpunktion.* By Dr. MARTIN PAPPENHEIM. Pp. 175. Vienna: Rikola Verlag, 1923.

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THE ENDOCRINE CAUSATION OF SCLERODERMA, INCLUDING MORPHŒA.

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Definitions.

Morphœa.—Morphœa is a localised form of scleroderma occurring in the shape of plaques or bands.

It occurs mostly in the female sex, especially those of neurotic temperament.(1) It may occur in childhood, or early or late in adult life, but most cases are recorded in the third and fourth decades.

Morphœa is essentially chronic in its course, the lesions making their appearance insidiously and developing slowly. If one excepts the moderate pruritus which may occur, especially before the lesions are fully developed, any subjective symptoms are of rare occurrence. The areas of predilection are at the base of the neck, both in front and behind, and also the upper portions of the chest and back, but lesions on the extremities are by no means uncommon. The essential lesion is either a small white spot or a band, this latter form being more commonly found upon the limbs. The colour varies from pure white to pearl or purplish white. In the case of plaques, they may be widely scattered and few in number, or they may be so close together that they may touch each other, and may be present up to the number of several hundred. The size may vary from a pin's head to a five-shilling piece, but the smaller spots are more common than the larger ones.

The appearance of the spots and their texture varies greatly, some being shiny and smooth, while others are wrinkled and dull. They may be raised above the surface of the surrounding skin; they are usually sharply circumscribed, and have the appearance of having been embedded

into the skin "like a mosaic." Occasionally hairs may protrude from the spot, and it may contain one or more horny plugs.

Scleroderma diffusa.—Scleroderma is an acute or chronic disease or group of diseases, characterised by a more or less diffuse hardening of the skin and subcutaneous tissues, often ending in atrophy.

The onset of the disease is frequently ushered in by a feeling of malaise. Chills, sore throat and pains in the joints are not unusual accompaniments. The affection may appear almost suddenly over a large portion of the skin, or it may spread so slowly that it is a long time before it is noticed. The affected skin becomes rigid, tense and hard, and its temperature falls a degree or two.(2) The skin appears œdematous to the touch, it pits occasionally, and cannot be pinched up or lifted from the underlying muscles. Where the disease spreads to the skin covering a joint the latter becomes immobilised. If the face is involved the countenance is expressionless, and the patient has the greatest difficulty in smiling or opening his mouth. At first sight the skin does not seem to be much altered in appearance, but the natural folds and creases are obliterated. Sensation in the affected areas is usually unaltered, but there may be loss of the finer sensations of touch. The skin is dry, due to the obliteration of the sweat-ducts, although at the commencement the sweating may be excessive and even result in the formation of bullæ.

The general health is usually good, but the patients may feel the cold greatly. In some cases the disease, by spreading to the thorax, interferes fatally with the mechanism of respiration.

In the atrophic form the preceding picture is followed after a variable time by a shrinking of the skin, which becomes ivory white in colour. The distribution is usually not so extensive as in the infiltrated form, only the face and upper parts of the thorax and arms being attacked in many cases. The skin is stretched tightly over the bones, the underlying muscles atrophy with great shrinkage of the limb, the joints are fixed and the hands are distorted.

The tendency in the infiltrated form of the disease is to gradual soften ing of the skin and recovery with occasional relapses. The atrophic form is more chronic, the condition persisting for years, and often terminating in death from exhaustion. Sudden death is fairly frequent. The hardness of the integument may disappear, but in many instances the underlying tissues may never recover their normal state.

The disease usually runs a more acute course in children than in adults.

On the Unity of Scleroderma, Clinical and Histological.

The fact that these diseases are very closely allied in their nature, as well as in the form of their cutaneous manifestations, that certain of the symptoms usually present are common to both affections, and finally that these manifestations may occur either simultaneously or at different periods in the course of the illness upon the same patient, can admit of no question.

There is a very close clinical affinity between the various forms of scleroderma and morphœa, because either the actual underlying process is the same in both diseases, or the end-product is the same; in both cases it is the formation of scar-tissue. The final solution as to their identity can only be obtained by the study of histological sections cut from the various stages and forms of the diseased skin. It is difficult to quote authorities on this subject for several reasons, the chief of which are:

(1) The dearth of comparative descriptions.

(2) Study of the histological literature shows that opinions are given rather than facts from which to draw any reasoned deductions.

(3) The imperfections of the older histological technique. This is exemplified by the paucity of information available as to the employment of the many differential stains which are of the utmost importance in the study of the histology of the skin.

The confusion that still exists may perhaps be explained by the fact that sections cut from the various lesions of scleroderma differ to a considerable extent according to the age of the lesion. It can be readily understood that a section taken from an old-standing case of morphœa differs in many important points from one taken from an acute case of infiltrating scleroderma; if, however, the same morphœa lesion is compared with one from a chronic atrophic scleroderma, the differences are very slight indeed. Most authorities agree that the infiltrating and the atrophic forms of scleroderma are one and the same disease, but the difficulty in acclaiming the circumscribed and the diffuse to be the same appears to arise chiefly from the totally different clinical picture presented by the two diseases.

The following authorities consider morphœa and scleroderma diffusa to be the same disease on clinical grounds:

Montgomery and Ormsby [3] state that morphœa clearly belongs to

the scleroderma group, showing lesions that have been recognised, though not commonly, in early lesions of scleroderma: it should be considered as a localised form of scleroderma.

Petges [4] states that morphœa should be grouped with scleroderma —everything points to it being a scleroderma.

Wilmot Evans [5], Malcolm Morris [6], Duhring [7], Stelwagon [8], MacLeod [9], Sequeira [10] and Schamberg [11] all agree that the two diseases should be grouped together. Unna [12], on the other hand, says that "a review of cases of scleroderma shows that the histological investigations correspond to the clinical, and that a uniform view of scleroderma is no more supported anatomically than clinically and prognostically. The common link which combines them all is the hypertrophy of the collagenous tissue, while the inflammatory appearances indicated by cellular growth and dilatation of the vessels are different in form and degree in each."

Histologically there is less agreement than clinically, but this may be explained by the reasons given above, and also by the scantiness of the descriptions.

Darier [13] believes that "the lesions of scleroderma, no matter of what clinical form, consist of a thickening, with partial disappearance or sometimes a degeneration of connective-tissue bundles; the elastic fibre plexus is preserved, and appears increased as a result of close approximation of the fibres. In recent cases of generalised scleroderma and sclerodermic patches I have demonstrated a subacute perivascular inflammation and a new form of connective tissue. The vessels were almost invariably found to be affected by endoperiarteritis and phlebosclerosis; the peripheral nerves are slightly involved or their sheath thickened."

'The papillary body is flattened and obliterated; the epidermis is often atrophic; the horny layer is increased. The follicles and glands disappear; sclerosis of the hypoderm and of the muscles has been described, with inflammation of the periosteum and rarefaction of the bony substance; incongruous lesions of doubtful significance are found in the nerve centres."

Bunch [14] says that perhaps the most consistent findings are those describing the epidermis, for in most cases the horny layer is thickened and the papillæ partly or entirely obliterated, while there is usually thinning of the rete. But the corium may either show hypertrophy of

the collagenous tissue, or degeneration of the connective tissue. The blood-vessels may be dilated or constricted.

Savatard ([15]), in discussing morphœa, states that "recent papules showed in the epidermis obliteration of interpapillary pegs, slight thickening of the horny layer with thinning of the granular layer of the rete Malpighii. In the corium the pars reticularis is practically occupied by a mass of collagenous tissue. Elastic tissue is present just beneath the epidermis. There is no evident cellular infiltration about the vessels."

Prof. Hubert M. Turnbull has examined portions of skin from one example of each of the two conditions in patients who have attended the London Hospital. To my request that he should give me his opinion upon the comparative pathology of the two conditions, he has kindly sent me the following answer :

"I have looked through the reserved sections of the portions of skin from the elbow of F. M—, a female, aged 24 years (S.D. 8, 1922), sent to me with a diagnosis of *scleroderma diffusa*, and those from the abdominal wall of J. W—, a female, aged 55 years (S.D. 603, 1915), sent to me with a diagnosis of *scleroderma guttata*. I have also read my reports upon these two cases, for which were employed sections stained by other special methods. . . . In Case 8, 1922 (scleroderma diffusa), the chief features are: very great pigmentation of the epidermis and of the subjacent dermis; collagenous fibres of the dermis found on measurement to be slightly thicker than in six controls, but quite normal in arrangement; elastic fibres perfectly normal in number and distribution; a slight perivascular infiltration (mast-cells, plasma-cells and lymphocytes); a similar infiltration round some of the hair-follicles; excess of horn in hair-follicles, especially in widened orifices.

"In Case 603, 1915 (scleroderma guttata*): No pigmentation. Focal, narrow strips of the papillary and subpapillary zones, and also large lenticular areas including these zones and extending deep into the dermis, occupied by dense homogeneous fibrous tissue in which almost all the elastic fibres have been destroyed. These areas resemble dense scar-tissue. Epidermis narrow and devoid of interpapillary processes over these sclerotic areas. Widened vessels in some of these areas. Hyaline fibrosis of walls of some capillaries. Some areas simply rings round capillaries. Dilated vessels and areas of abundant infiltration (fibroblasts, lymphocytes and plasma-cells) in remainder of upper part of dermis. No recognisable hair-follicles and sebaceous glands, but some groups of foreign-body giant-cells which doubtless are removing some epithelial appendage. Cystic dilatation of sweat-ducts below the sclerotic areas.

"In Case 603, 1915, said to be one of scleroderma guttata, the sclerosis of the dermis is evidently the result of a replacement of the outer collagenous and elastic fibres of the dermis by a dense, inflammatory scar-tissue. The inflammation is conspicuous and appears to be essentially perivascular.

* Full report published in the *British Journal of Dermatology*, 1915, xxvii, p. 462.

"In Case 8, 1922, said to be one of scleroderma diffusa, if there is any sclerosis of the dermis it is due to a thickening of the collagenous fibres without any disturbance of their normal arrangement, and without any destruction of elastic fibres. The feature of this case is melanotic pigmentation of the skin.

"In both cases there is inflammatory infiltration of a chronic type. In Case 8, 1922, this is very slight and is perivascular and perifollicular. In Case 603, 1915, the infiltration occupies large areas and is associated with vascular dilatation. The infiltration does not surround a group of sweat-glands, so that it may possibly be confined to the same distribution as in Case 8, 1922.

"It is possible that the strip of skin sent from Case 8, 1922, was in reality not yet sclerotic, and would in course of time have suffered a scar-like sclerosis, such as was seen in Case 603, 1915. I was told that it came from a sclerotic patch and included also normal skin. We examined the whole strip (three sections), and found no essential variation in the appearances.

"In conclusion: in the specimen of 'scleroderma guttata' the processes are definite and can be interpreted. In the specimen of 'scleroderma diffusa' I found no satisfactory explanation of the sclerosis said to have been observed clinically. Measurements certainly showed the collagenous fibres to be slightly thicker than in controls, but a process of thickening of fibres without other alteration is difficult to understand, especially when there is also evidence of inflammation, even though slight. For this reason I refused to express an opinion upon the nature of the process. It is obvious, therefore, that I cannot express an opinion upon the differences or resemblances in the pathological processes in these two clinical conditions until I have examined more material—at any rate, more specimens of scleroderma diffusa."

Historical.

The first case of scleroderma diffusa which is on record was under the care of Signor Crusio at Naples in 1752. His account of the disease and the various remedies which were tried and resulted in a cure makes very interesting reading.

The First Histological Description.

Crocker, in 1879, was the first to cut sections of scleroderma, and the following is an abstract of his findings.

Epidermis.—Unaltered except for pigmentation and occasionally a few wandering leucocytes. *Corium.*—Papillæ less prominent than usual. Thrombi in the cutaneous vessels. Perivascular leucocytic infiltration. *Glands.*—Ducts obliterated by fibrous tissue. *Vessels.*—No lardaceous changes apparent in the vessel walls. Areas of dilated cutaneous vessels.

The process in scleroderma is identical with that occurring in morphœa, except that the former occurs on a deeper plane.

The First Post-mortem Examination of a Case of Scleroderma. ([17])

In 1878 Chiari described a complete post-mortem examination of a case of scleroderma diffusa, the findings being as follows :

Complete adhesion of the layers of the pleura and pericardium. Fatty degeneration of the myocardium. Universal marasmus and anæmia. Scleroderma. Microscopic examinations of the skin and various organs were made, but nothing abnormal was found except the usual changes in the skin which are associated with scleroderma.

The author assumes that a chronic inflammation of the skin is the primary cause of scleroderma.

Authors Discussing the Thyroid Causation, with Cases.

Osler ([19]), in a paper written on eight cases of scleroderma, comes to the conclusion that "thyroid extract has certainly not the same specific action in scleroderma as it has in myxœdema. In none of these cases did the skin of the affected areas become softer or regain its natural appearance. In two of the cases the disease did not progress under its use, but that is the best that can be said from my own experience."

"Altogether my personal results and those recorded in the literature do not favour the treatment of the disease by thyroid extract."

Case 1.—Recurring arthritis before onset; diffuse scleroderma; sclerodactylism; trophic lesions; no enlargement of the thyroid; claw-hand; all the skin affected except that of the abdomen. The condition of the toes suggests Raynaud's disease. No articular thickening, but the skin over the joints is glossy and hidebound. No increase in skin-pigment.

Case 2.—Diffuse scleroderma; onset with stiffness and swelling of the hands and feet; possible arrest under the use of extract of thyroid. Face slightly involved. Thyroid not palpable. No involvement of thorax. Arms involved; great congestion if held down. Claw-hands; nails unaltered.

Case 3.—Arthritic pains; diffuse scleroderma of arms, hands and shoulders; erythema of skin over knees; brawny œdema of legs; pigmentation. Death with gastro-intestinal symptoms. Face unaffected; claw-hands; pigmentation; pain on movement; swelling of legs; thyroid not palpable.

Case 4.—Pulmonary tuberculosis; scleroderma of neck and back, of chest and of upper abdomen. No pigmentation; no vasomotor changes; muscles of shoulder girdle involved.

Case 5.—Advanced stage of Graves's disease; remarkable scleroderma of both legs. Death from heart-failure. No disturbance of sensation; no pigmentation; thyroid of medium size with marked pulsation and thrill.

Case 6.—Onset with vasomotor changes in arms and legs; gradual scleroderma of fingers, with areas of necrosis on the finger-tips. Great improvement with thyroid extract.

Case 7.—Scleroderma of the hands and fingers; tachycardia; extraordinary cyanosis of the skin of the legs. Face slightly affected; claw-hands; severe venous congestion of the legs; cardio-vascular system normal except for a pulse-rate of 138 in the erect position. Sudden death.

Case 8.—Diffuse scleroderma; intense general pigmentation with patches of leukoderma; swelling of the inguinal glands; progressive advance of the disease. Claw-hands; face affected. Administration of thyroid extract was ineffectual.

Roesch ([20]) reports a case of generalised scleroderma in the indurated stage in a young woman with symptoms of abnormal thyroid and supra-renal functioning. He concludes therefore that scleroderma may possibly be caused by disturbances of function of one or more glands of internal secretion.

Because two diseases are associated together, it certainly does not follow that one is the cause of the other, and the conclusions that Roesch draws may be quite correct, but they are certainly not justified by the evidence produced.

Scleroderma diffusa in a girl, aged 9 years. H. Goodman ([21]):

Seven months previously suffered from tonsillitis. Operation at age of seven months for intestinal trouble. The disease started with involvement of the face, the patient being unable to open her mouth as widely as usual. Neck, scalp, face and arms were affected. Pulse 140–110. Temperature 99° F. Blood-count normal. Wassermann reaction was doubtful. Urine contained albumen.

Recovery under the use of thyroid extract.

Goodman concludes: "The consensus of opinion to-day with regard to the ætiology of scleroderma is that the affection is at least closely related to disturbances of function or 'unbalance' of the secretion of one or more so-called ductless glands."

In this case there seems to have been no symptoms which could be attributed to a disordered action of the thyroid, except, perhaps, the rapid pulse-rate. The opinion stated at the end of the case may be quite correct, but the case does not appear to contribute any strong evidence in its favour, since scleroderma has a tendency to spontaneous recovery in certain cases, irrespective of the treatment adopted.

Hartzell ([22]) considers that many cases of scleroderma are due to some pathological change in some of the ductless glands, particularly in that of the thyroid. This is merely an opinion, and Hartzell has not brought forward any evidence to prove its correctness.

Dittisheim ([23]) states that scleroderma, associated with Graves's disease,

is particularly common in Zurich. Out of seventeen cases of Graves's disease, eight had scleroderma. The association of Graves's disease with scleroderma in such a large proportion of Dittisheim's cases is very interesting, but it is contrary to experience in this country.

Singer ([24]) believes that scleroderma usually occurs in connection with disease of the thyroid gland, which he has found affected in many cases. This statement is not according to clinical experience, and does not appear to be correct.

Leube ([25]) states that he has frequently observed scleroderma in Graves's disease as a complication.

Grünfeld ([26]) reports a case in a woman, aged 33 years, associated with Graves's disease of many years' duration. Extensive areas of scleroderma developed, but under thyroid gland treatment both the exophthalmic goitre and the scleroderma disappeared completely.

The reports of Dittisheim, Leube and Grünfeld of the association of Graves's disease and scleroderma seem to indicate some common cause for these two diseases. It cannot be merely coincidence that these two diseases are found together in so many cases.

Sequeira ([27]) reports four cases of scleroderma (all of them in females) associated with disease of the thyroid. In discussing the pathogenesis of scleroderma, the author states that this affection occurs in connection with such a variety of conditions that it is difficult to believe that many of the casual relationships which have been suggested can be accepted.

While it is true that a certain proportion of the cases are associated with affections of the thyroid, nevertheless there is nothing to warrant the conclusion that alterations in the activity of the gland or its secretion are actually causative of scleroderma. The very fact that scleroderma has been known to occur both in thyroid hypertrophy and in thyroid atrophy makes one cautious.

Atwater ([28]) reports a case which he treated with thyroid extract with no improvement. The patient was given thyroid extract, but after two months' treatment she was worse than ever.

Cockayne ([29]) described a case of scleroderma in a premature child, born at the eighth month, weighing $2\frac{1}{2}$ lb. The skin was indurated, hair was abundant, but fell at four months, the child becoming almost bald.

Hydrocephalus was present. When first seen at seven months the infant showed a typical scleroderma and sclerodactyly of the adult type,

with some fibrous myositis. The fingers were firmly flexed, remarkably small, and with a wax-like appearance ; the nails were atrophic.

The skin of the scalp was thick and shining, with a sparse covering of fine hairs ; eyebrows and lashes were almost absent.

Two years later there was little change noticed.

The child was very subject to nasal discharge, conjunctivitis and blepharitis, and at the age of $1\frac{1}{2}$ ulceration of the cornea took place in both eyes. Nystagmus and inequality of the pupils subsequently developed.

The Wassermann reaction was negative.

Treatment with mercury was tried for six months, and thyroid extract for a longer period, with no results.

Dercum ([30]) considers it to be probable that when improvement does follow the use of thyroid extract in scleroderma, the effect is to be attributed not to action upon the swollen and infiltrated skin, but upon the subcutaneous fat, and that it materially hastens the atrophy and disappearance of this tissue in the atrophic form of the disease.

The co-existence of serious disease of the thyroid gland with scleroderma naturally suggested treatment of the cutaneous condition with thyroid extract.

Roques ([31]) collected 67 cases in which this had been done, and the results were as follows :

Cures	4 = 5·97	per cent.
Improved	32 = 47·0	,,
No effect	31 = 46·0	,,

Graham Little ([32]) showed a case in 1916 before the Royal Society of Medicine of scleroderma associated with Graves's disease, and later with myxœdema. The patient benefited considerably by implantation of human thyroid into bone-marrow.

Female, aged 52 years, the wife of an officer.

In 1902 suffered from tachycardia, anæmia, dilatation of the heart and (?) neuritis of the hands and shoulders.

In 1907 her thyroid appeared normal, but Sir Thomas Barlow considered that her symptoms pointed to a "half-developed" exophthalmic goitre. Her hands were puffed, stiffened and dead, and she also had brawny swellings below her eyelids resembling a chronic urticaria. Pigmentation was well marked.

In 1908 the diagnosis was altered to that of myxœdema, and she was given thyroid extract. Later in the year her thyroid enlarged, her pulse was 120, anæmia was well marked, and her heart was "murmurish." She suffered from periods of irregular fever with urticarial swellings; also from very severe pains in the shoulder and neck, and a (?) fibrositis of finger-joints, elbows and shoulders.

In 1909 she developed parotitis, first on one side and then on the other; there was no suppuration, but she had pain and difficulty in moving her jaw. These attacks were frequently repeated during the next eighteen months.

In 1910 scleroderma was present, affecting her fingers, forearms, face and thighs, and so she was practically crippled. She went to Droitwich and then to the sulphur baths at Biskra, and from there she went to Kocher, to whom Sir Thomas Barlow wrote concerning her thyroid:

"On the whole my opinion is that it has shown some degree of atrophy, but it is not easy to say how far the wasting is proportional to her general wasting (which was very marked). She has had very considerable anæmia with a certain amount of pigmentation. This has been very severe at times—almost bad enough for a pernicious anæmia. As for treatment, it cannot be denied that at times some benefit has resulted from thyroid extract, but it has never been considerable, and I am of the opinion that at times it has exhausted her. I have never seen a case of pure myxœdema behave like this."

In May, 1911, Kocher removed a piece of thyroid from a goitre, and immediately transferred it to the bone-marrow of her tibia through an incision on its anterior surface. Seen one month later, her colour was better, her movements were freer, but she could not move her jaw owing to the immobility of the skin of her face; her scleroderma was much better.

In February, 1912, Kocher operated again, and inserted the graft into the other tibia. She developed a right lobar pneumonia and nephritis with 25 per cent. albuminuria.

In June, 1913, she became very ill with pyorrhœa alveolaris. She was treated with considerable benefit by vaccines.

In September, 1913, she had an attack of herpes zoster. Her teeth were then all removed. Since then there has been a remarkable improvement, which has been maintained.

This is an extremely interesting case, and one which, at first sight, would incline one towards the thyroid origin of scleroderma. However, the removal of septic foci, by extraction of the teeth, appears to have been of more benefit than the grafting of new thyroid tissue.

Hektoen ([33]) considers the relation of the thyroid to myxœdema is important in this connection. The changes in the skin vary in myxœdema, but it seems established that the elastic tissue is increased, and the collagenous tissue is diminished. He concludes that if athyreosis can produce such changes, there can be no inherent reason why dysthyreosis, due to various causes, may not lead to scleroderma.

Barber ([34]) showed a case of morphœa with cystic enlargement of the thyroid and signs of hypo-thyroidism at the Royal Society of Medicine. The case was that of a woman, aged 53 years. At the age of 30 she began to put on flesh and her hair thinned. She felt the cold keenly. Her eyebrows were thinned.

There were two patches of morphœa at the back of her neck.

Authors Discussing Pituitary Causation of Scleroderma.

Schwartz ([35]) has had six cases under his observation, all of whom showed increased sugar tolerance. Some took up to 450 grm. of glucose without passing glucose in their urine. All had been given pituitary extract,* and although none of his cases had been under treatment for a long time, all showed definite improvement.

This report would be more valuable if the cause of the increased sugar tolerance had been worked out. As it is, it contains little of scientific value. No X-ray of the sella turcica is mentioned.

Trimble ([36]) reported success with the administration of the anterior portion of the gland.

Izar ([37]) advises in cases of scleroderma an investigation into the functions of the endocrine glands, not only in the patient, but also in other members of the family, endeavouring thus to find out which of them is below standard.

In this way he deduced that the pituitary was primarily responsible for the scleroderma in a girl of 7. The sella turcica was rather larger than normal for the child's age (7 mm. in height and 19 mm. in diameter). The girl presented a localised scleroderma on the right hand, rapidly spreading to the rest of the body, being more marked on the neck and thorax. The cutaneous thickening was so great that the child resembled a wax doll. Provocative injections of epinephrin, atropin, thymus, ovarian and thyroid substances produced no reaction. On the contrary, the injection of ·25 and ·5 c.c. of pituitary extract produced a rise in temperature, increased blood-pressure (from 70 mm. to 108 mm.), and caused the pulse-rate to become slow. With this positive reaction a course of pituitary extracts was started, with the result that after the sixth daily injection the scleroderma began to recede.

By the 49th day, after 16 injections each of pituitrin and hypophysin, there only remained some pseudo-œdema on the neck, forearms and legs, and the treatment was continued by the administration of half a tablet of hypophysin on alternate days by mouth.

All signs of the skin affection had disappeared by the end of six months.

The striking and beneficial action of this organo-therapy would seem to establish without doubt the pituitary origin of the cutaneous lesion in this case.

* Dose: B. & W. pit. extr. 6–18 gr. daily.

The difficulties of X-ray technique make one rather dubious of accepting these measurements of the sella turcica. This is undoubtedly a very good case, and one which tends towards the acceptance of the theory of a derangement of the ductless glands as a cause of scleroderma, but one would have preferred to know if there were any other signs of pituitary disorder, such as glycosuria or increased sugar tolerance, and also whether any other investigations were made, except the one injection of pituitrin, to establish the fact that the pituitary was disordered.

Heimann ([38]) reported a complete cure of scleroderma by the use of pituitrin.

Strumpell ([39]), in discussing acromegaly, says

"In examining cases of typical scleroderma I have often noticed a resemblance between these two diseases. To explain briefly what I mean, I would point out that in both diseases the part that is first attacked is the lower part of the face (nose, mouth and chin). Whilst in acromegaly the skin becomes hyperplastic and there is some increase in the size of the bones, in scleroderma the skin is atrophied, and the bones of the affected areas become so thin that there is even necrosis (when the terminal phalanges are affected).

"So while in acromegaly we find progressive hyperplasia, in scleroderma there is progressive atrophy. I do not suggest a common origin for these two diseases (such as myxœdema and Graves's disease), but I wish to draw attention to this possibility. I consider that a post-mortem on a case of scleroderma should always include the pituitary."

Roux ([40]) reports the following case :

D. T—, a miner, always very strong, not a day's illness in his life. Denies syphilis.

Nine years ago, after exposure to excessive cold, his feet were frost-bitten ; he lost none of his toes. The following winter he had numerous chilblains, and at the same time his toes began to shrivel up, with the formation of numerous ulcers. There was no bone necrosis. He was admitted to hospital several times, but the process in his feet continued and was always worse in cold weather. He had great pain.

During the past three months new symptoms have appeared. On 3 or 4 days each month he becomes jaundiced, his sight fails, and objects swim before his eyes. He often falls, but never loses consciousness ; he has no convulsions and he gets up alone at once.

Both feet, outer side of calves, inner side of thighs, right side of abdomen, all the back, arms, forearms and hands show the following :

Complete loss of hair, smooth normal coloured skin (except on the abdomen, where there are scratch marks). The skin feels like leather. Sensation to pain and touch is diminished, also that to heat ; that to cold is normal.

The toes are markedly deformed and ulcerated.

X rays show the bones to be normal.

The pulse is slow, and permanently at 40, also jaundice, giddiness and fainting attacks are present.

The stethoscope proved a cardiac rate of 80.

On being given extr. thyroid the general condition improved at once, but not the skin.

One month later pituitary injections were started, but unfortunately the man died of septicæmia from a place on his foot.

Post mortem: No naked-eye change in the viscera. The pituitary showed great congestion and hæmorrhages under the capsule, both old and recent. The centre of the gland showed degeneration and chronic inflammation.

Touchard ([31]), although he believes that an intermittent secretion of adrenalin is a symptom of scleroderma, claims that it is not entirely due to affection of the blood-forming glands. All the disturbances of vaso-motor origin, as angioneurotic œdema, erythromelalgia, sclerodermia, sclerodactyly, Raynaud's disease, can be considered as related in the ætiological origin. Nearly all authors agree that one of the exciting causes of scleroderma is a sudden change of temperature—a sudden exposure to the cold. In one case the patient was caught in a thunder-storm and remained the rest of the night with his wet clothes on. From this time he began to suffer from paræsthesia, and gradually the skin of his extremities began to show hardening. Scleroderma is the result of a disturbance of the internal secretions, with increased tonus in the sympathetic. The central point of distribution through the system of the chromaffines is the hypophysis, and it is very likely that in disturbances of this organ is found the true reason for scleroderma.

The protracted contraction of the blood-vessels under the influence of a vaso-constriction and the consequent ischæmia in the area of the blood-vessels, together with the injurious influence of the adrenalin-like substances on the tunics of the blood-vessels, easily explain the pathological alterations in scleroderma, and the degenerative and chronic inflammatory nature.

Touchard is in error when he states that the hypophysis is the central point of distribution through the system of the chromaffines. There is no chromaffine tissue in the pituitary; this is only found in the suprarenal bodies, the carotid body, and the sympathetic ganglia. It is by no means established that a sudden change of temperature is one of the exciting causes of scleroderma, nor are the physiologists in agreement that a sudden shock will produce an excess of adrenalin in the blood.

Gaskill [42] says that he has found that not only are there changes in the thyroid, but also in the pituitary.

Ravogli [43] describes a case of scleroderma, and then proceeds to discuss the ætiology as follows :

In this case the skin began to show alterations together with neuralgic pains of the peripheral nerves. It may be possible that an affection of the suprarenal glands and the hypophysis would produce alterations in the nutrition of the skin by their disturbed equilibrium. In some cases the pigmentation is associated with disease of the suprarenals due to adrenalinæmia. The adrenalin when carried to the surface of the skin is oxidised and precipitated, and the discoloration is the result of the products of oxidation. It is also possible and more probable that from a spastic contraction of the blood-vessels, the colouring matter of the blood is forced out of its tunics, and infiltrates the tissues of the skin. The hypophysis has been considered a factor in scleroderma ; Strumpell believes in a diminution of its function, while others believe in an exaggerated function. It is maintained that a disturbed function, either in excess or in defect, is the result of anatomical alterations in the gland. Scleroderma and acromegaly have been found in the same patient, and acromegaly means hyperpituitarism. Scleroderma has also been ascribed to an affection of the sympatheticus, which causes disequilibrium in the secretion of the glands, and produces changes in the skin. Scleroderma has also been found in association with paralysis agitans, which may be the result of disease of the parathyroids.

In these cases of scleroderma, it seems that the blood contains in excess, materials which have vaso-constrictor action. This, however, has not been proved, and the only explanation is that adrenalin-like substances are not constantly increased in the blood, but that their increase is only temporary and in alternating spells.

Ravogli has given a great deal of pure theory, and his article contains several mis-statements of facts. Paralysis agitans is believed to be entirely a disease of the central nervous system, a degeneration of the basal ganglia, and is not now connected at all with the parathyroid glands, although administration of these glands may ameliorate its symptoms. Addison's disease, in which there is an acknowledged suprarenal deficiency, is not associated with spasm of the blood-vessels.

Authors supporting Suprarenal Causation of Scleroderma.

Winfield ([11]) describes a case simulating Addison's and Raynaud's disease, which showed marked improvement from the administration of suprarenal extract.

Female, aged 52 years, widow, one child, no miscarriages.

Prior to September, 1902, her health had been good, but about then her hands frequently became cold and swollen.

In January, 1903, her wrist- and finger-joints became stiff and swollen.

In April, 1903, she had pleurisy and a slight discharge from her umbilicus. From that time her skin grew harder and darker, and her wrist- and finger-joints became almost immovable. Her ring fingers were very swollen, and there was a discharge from the terminal phalangeal joint.

The whole of her skin was coloured, her tongue was dry, her bowels not open, and her general condition was very bad; she complained greatly of pain, cold and sleeplessness.

She was treated with desiccated suprarenal, making an immediate and continuous improvement, except for a short interval when the liquor was substituted for the desiccated gland.

And again :—

Child, aged 15 years, with scleroderma of three years' standing, with cold, stiff and discoloured hands; wrist-joints stiff and her fingers ankylosed, with trophic ulcers on them. Her face and feet were also affected.

She was treated with desiccated suprarenal, making an immediate and uninterrupted improvement.

Winfield has given two very good cases which were improved by suprarenal extract. However, it is a well-known fact that even in cases of well-established adrenal deficiency, treatment with the desiccated extract is of no value. Also it is no proof of the causation of a disease that it is improved by the administration of a gland extract.

Millard ([45]) had a case of generalised scleroderma: the fingers were markedly affected, being like drumsticks. Injections of adrenalin were attended with great success.

Increase in the pigment of the skin is sometimes a very striking feature of scleroderma. It occurred in 144 out of 508 cases collected by Lewin and Heller. ([46]) As a rule it is slight in degree and not wide-spread, but if pronounced, it raises the suspicion of Addison's disease.

Schultz ([47]) reports the case of a girl, aged 19 years, with sclerosis of the arms and legs and much muscular atrophy, with also pigmentation of the face and neck. The patient became extremely emaciated and feeble, and died suddenly four months after the onset of the disease.

Post-mortem : The left suprarenal was moderately increased in size, adherent to adjacent parts, and presented a few small greyish nodules.

A detailed histological account of the left suprarenal body would have increased the value of this report.

Lereboullet ([18]), not trusting to the use of the extract of one gland only, used thyroid, suprarenal and pituitary.

In the case of a man, æt. 17 years, an acute case of scleroderma, his face being like a mask, the cheeks looked as if they were glued to the skeleton ; the neck was hard and rigid, and it was impossible to take up a fold in the skin on the chest ; the hands were bluish, and the fingers immovably pressed into the palms. The upper part of the arms seemed to be the only parts which had escaped. Under treatment three years later with thyroid, pituitary and suprarenal extracts, all of which seemed called for by special symptoms, plus phosphoric acid and arsenic tonics, marked improvement was seen even in two months, and by the age of 24 the sclerodermic condition had entirely disappeared, and the general aspect of the young man was normal.

Other Ætiological Suggestions.

As the ætiology of scleroderma is not properly understood, it follows naturally that a large number of causes should be identified with the commencement of this disease.

It is only of recent years that the importance of the endocrine glands has been properly appreciated, and even now we seem to be only at the threshold of important discoveries, which, it appears certain, will elucidate the ætiology of many obscure conditions. But what is even more important than to be able to point to any particular gland as being at fault is being able to say with certainty what cause it was that brought about the failure of that gland, and so these suggestions by various authorities on the causation of scleroderma may be of service in indicating some ætiological factor, if indeed scleroderma can be traced to an endocrine causation.

Trauma.—Roberts ([19]) reports the case of a small boy, who at the age of two years fell against a fender and bruised his abdomen. A few weeks later the bruised area became indurated. During the two following years the morphœa advanced towards the right shoulder, not in direct continuation, but in isolated patches, separated by areas of healthy skin. Reaching the shoulder, it descended the arm, thence to the forearm and fingers, following the cutaneous branches of the median and ulnar nerves.

The index finger contracted, the thumb became stiff, and the skin between the finger and thumb rigid.

Bramwell ([50]) reported nine cases of scleroderma, out of which five occurred in stonemasons, and one in a miner and one in a coppersmith. All these men used cold chisels, and in all cases the disease started in the hands. None of the patients had had syphilis.

Dercum ([51]) reports the case of a man of 43, who was injured on the occiput by the falling of a block of ice. This was followed two months later by scleroderma, spreading from the scar round his face and neck and then over his shoulders, arms and trunk. Albumose was found in his blood.

Sequeira ([52]) reported the case of a youth, aged 18 years, who 4 years previously had injured himself by falling on some rails. He was severely bruised across the lower part of the left chest. Six months later he noticed an alteration in the colour of the skin of his left thigh and the left side of his chest. He then developed extensive morphœa, confined to the anterior and lateral parts of his chest and upper abdomen, all on the left side. He also developed an extensive band of scleroderma running parallel to the left sartorius and broadening out below the knee to include the front of the leg as well as its inner border.

A case was shown at the Dermatological Section of the Royal Society of Medicine on July 10th, 1922, in which a man who used a cold chisel developed scleroderma in his right middle finger; this spread over the whole of the distribution of the right ulnar cutaneous, and then appeared in the area of the middle cutaneous branch of the anterior crural of the right leg. In this case there seemed to be a mixture of traumatic and nervous influence, and it can be compared with Bramwell's cases.

Irritation.—Walker ([54]) ascribed one case to irritation. He had under his care a female, aged 17 years, who showed a long streak-like eruption commencing just below the angle of the jaw on the left side, and extending downwards and inwards. Two months previously the patient had had a stiff neck, and had painted it with iodine. It was doubtful whether the onset of the scleroderma had produced the stiffness, or whether the scleroderma had been produced by the application of the iodine.

Eddowes ([55]) reported a case of left hemi-atrophy of the face with a band of morphœa following the line of the left sterno-mastoid in a girl of 7 years old. The child was subject to severe pain in her teeth on the affected side, which the mother used to relieve with strong plasters of

pepper and with strong liniments. The morphœa started at the same time as the eruption of the first molars. The hemi-atrophy was presumably due to disuse.

Exposure to cold and chills.—Lewin and Heller ([56]) report the case of a girl, aged 17 years, who gave a history of cessation of menses, swelling of ankles, knees and wrists, following exposure to cold air eight months previously. There was a universal scleroderma. Death occurred from pleurisy and heart failure.

The same authors ([57]) reported a case of scleroderma in a child of $8\frac{1}{2}$, beginning in the neck with rapid spread. The onset followed a chill.

Shock.—A girl in Lewin and Heller's series ([58]), aged 5 years, was frightened by a runaway horse five months previously. Shortly afterwards she was frightened again by a sudden firearm salute in a cemetery. The child's character changed; she complained of a pain in the neck, and a sense of constriction on opening her mouth. Generalised scleroderma developed over the upper half of her body.

Dercum ([51]) reports the case of a woman affected with diffuse scleroderma following immediately on a fire in her house.

Infections.—Lewin and Heller include the two following cases:

A girl ([59]), aged 10 years, affected with diffuse sclerodermia over the upper half of her body, following a septic finger, which was complicated by bronchopneumonia.

A girl ([60]), aged 5 years, suffered with tonsillitis, pharyngitis, difficulty in swallowing, pains in her legs and a scarlet eruption of spots on her breasts abdomen and arms, of one day's duration. There was high fever and slight albuminuria. After the disappearance of these symptoms there was enlargement of the lymph-glands behind each ear. Three days later there was swelling of the eyelids. During the second week of her illness diffuse scleroderma developed.

Hoppe-Seyler ([61]), impressed with the occurrence of the disease in two children from the same place, suspected an infectious origin. No microorganisms have been demonstrated in the cases examined, but it is worthy of note that scleroderma has been seen as a sequel to scarlatina (Pringle), diphtheria (Marsh), erysipelas (Chauffard), tonsillitis, pneumonia, phthisis, influenza, malaria, and measles. He considers that Dana's ([62]) suggestion that any infectious disease may be followed by scleroderma is quite justified.

Goodman ([63]), discussing the ætiology of scleroderma, says:

"A great number of cases follow colds, exposure to wet and

draughts. Tonsillitis preceding many of the recorded cases, together with the fact that the neck is almost always the first part to be affected, leads one seriously to consider scleroderma diffusa as an affection spreading from tonsillar lymphatic tissue, through the lymphatics of the skin."

Crocker ([64]) admits the possibility of a nervous origin, especially in cases of fifth nerve affections. Prolonged anxiety and worry are usually found. The frequent association of scleroderma with acute rheumatism and peri- and endocarditis, without other rheumatic symptoms, and the history of cold and wet so often met with preceding the onset, suggests some blood change is concerned in the production of the lesion ; perhaps the increase of fibrin in the blood, which characterises acute rheumatism, may be a favouring condition. Symptoms and localisation of the process in the perivascular sheaths present a close analogy to phlegmasia alba dolens, where the thrombosis in the veins, with inflammation of the lymphatics, leads to similar whiteness and hardness of the limb ; but here the deep trunk vessels, and therefore the whole limb, are affected, while in scleroderma, with a similar tenseness, it is mostly limited to the deep parts of the skin and the immediately adjacent tissues. A general inflammation of the deep part of the corium, and perhaps of the fat, with consequent lymphatic and vascular blocking, seems a feasible explanation, though it does not negative a possible nervous influence.

Crocker ([65]) reports the case of a child of 12 years in whom the whole body surface was involved except the palms and soles within a fortnight. There was also endo- and pericarditis present.

Lymphatic obstruction.—Heller ([66]) supports Kaposi's hypothesis that scleroderma is due to general or local lymphatic obstruction. In support of this he quotes a case associated with obstruction of the thoracic duct.

Congenital.—Langmead ([67]) reports the case of a boy of 4½, the last child of a family of three ; the boy was born when his mother was 42 years old. At birth the child was apparently healthy, except for a discoloration and rash present on the knees, face and hands. The child was a moderately marked example of the mongolian type of amentia, but with mental capacity above the average in these cases. All the limbs showed scleroderma, and the X-ray showed the subcutaneous tissue in the thickened areas to be sprinkled with small pleomorphic calcareous deposits.

Cockayne ([68]) considers it a very rare condition to find in the newly

born. "Some cases have been described as congenital scleroderma which are really instances of annular fibrous constriction, probably caused by pressure from amniotic bands or coils of the umbilical cord. These are not very uncommon, and are usually accompanied by other congenital defects."

A true congenital case is reported by Haushalter and Spillman ([69]) in a female infant in which the whole of the left leg was affected. The same authors record sclerodactyly in two sisters, aged 7 and 2 years, in whom the disease was first noticed at the ages of 5 and 6 months respectively.

Engelmann ([70]) saw a girl, aged 7 years, in whom the scleroderma was first seen at the age of 3 months, and spread widely over the face, trunk and limbs, causing a secondary atrophy of the underlying muscles.

MacLeod ([71]) reports a case occurring in mother and daughter, both having morphœa.

Pregnancy.—H. Fox ([72]) described the case of a woman, aged 25 years, who noticed pigmentation on the left side of her face when she was five months pregnant. This was her first pregnancy. The left cheek then increased in thickness. Pigmentation and thickening remained stationary for 22 months. Her general health was good.

Intestinal toxæmia.—Schwerdt ([73]), on the assumption that scleroderma is the effect of an intestinal toxin, which the affected mesenteric glands cannot neutralise, gave the gland extract with great success in certain cases.

Syphilis.—Schamberg ([74]), in discussing a case of scleroderma in a man, aged 23 years, said that he felt that as long as so many of these cases showed a positive Wassermann reaction he could not help thinking they were nearly all syphilitic in origin.

Jackson ([75]) in 1909 showed the case of a child, aged 6 years, with scleroderma, and her mother with a positive Wassermann reaction.

Brocq, Fernet and Maurel ([76]) reported a case of diffuse and rapidly spreading scleroderma in the course of a secondary syphilitic infection.

In 1910 Whitehouse ([77]) was investigating the Wassermann reaction, and found that out of five cases of diffuse scleroderma, three gave strongly positive, one faintly positive, and one a negative Wassermann reaction.

Hutchinson in 1884 showed that syphilis could produce an ascending arteritis resulting in Raynaud's phenomena.

The first clinical links in the chain are supplied by the abundant

evidence uniting Raynaud's disease with scleroderma, one of which links was recognised by Grasset in 1878—some years before Hutchinson's observations.

Association with Raynaud's disease.—Favier ([78]) quoted fourteen cases where scleroderma and Raynaud's disease were associated, and concluded that there was often a close relationship between the two affections, and that it was often impossible to separate one from the other.

Grasset ([79]) considers that—"There is no other conclusion than that there is a close affinity between scleroderma and asphyxia localis."

White ([80]) had a lady of 44 under his care who had scleroderma in various parts as well as Raynaud's disease and rheumatism.

Hutchinson ([81]) draws a very close comparison of Raynaud's disease with scleroderma. He gives many cases illustrating the comparison.

Arsenic.—Ayres ([82]) reports three consecutive cases of diffuse scleroderma, all of which showed arsenic in the urine. He tabulates the symptoms common to the disease and to arsenical poisoning, pointing out the points of resemblance, *e. g.* neuritic symptoms, pigmentation, skin changes, loss of weight, areas of involvement, gastro-intestinal symptoms, onset, vaso-motor disturbances, muscular weakness, and occasionally anæmia.

Nervous.—Lewin and Heller ([83]) consider scleroderma to be a trophoor angio-neurosis caused by changes in the nervous system.

Cockayne ([84]) believes scleroderma to be a trophoneurosis due to disease of the sympathetic system. The prodromal signs and symptoms—erythema, pains, pigmentation and transient attacks of local cutaneous asphyxia—which commonly occur are in accord with this view, as are the attacks of Raynaud's disease which often precede sclerodactyly.

The distribution of the skin lesions often corresponds to segmental areas, spinal areas, and to the course of the cutaneous nerves. The coincidence of the sclerosis with hemi-atrophy of the tongue, face or whole body, and the association with organic nervous disease, such as tabes, afford further evidence of nervous origin.

Many cases have been met with in which scleroderma and disease of the ductless glands have affected the same person. Myxœdema, Graves's and Addison's diseases have all been seen with scleroderma. In such cases the disease of the skin and the ductless glands are probably due to a disorder of innervation.

The cardiac, respiratory and gastric crises associated with scleroderma

can be interpreted most satisfactorily in the same way. The cases of scleroderma with sclerodactyly, and accompanied by myositis, are more probably due to a local infection of the skin or of the skin and muscles.

Jacquet ([85]) has described changes in the cord " myelite cavitaire " in scleroderma, but Mott ([86]) failed to find any evidence of disease.

Steven ([87]) found atrophy of the grey matter of the anterior horn-cells of the cord on the same side as an area of localised scleroderma.

Brissand ([88]) maintains that the skin affection depends on disease of the sympathetic system.

Hutchinson ([89]) describes many cases of scleroderma, and believes that it is due to nervous causes. He particularly draws attention to several cases of scleroderma affecting the distribution of the fifth nerve and compares it to herpes zoster.

Streatfield ([90]) considered the disease to be of nervous origin and described a case of morphœa limited to the fifth nerve with exostosis.

Out of seventeen cases gathered by Josephovitch ([91]) of hemi-scleroderma, three were his own. According to him particular attention should be drawn to the following case :

In a child, aged 4 years, convulsive attacks appeared in the muscles of the right half of the body, beginning in the muscles of the right half of the face; these attacks seemed to belong to the Jacksonian type of epilepsy. One and a half months later there appeared an anæsthesia of the muscles of the right side of the back and a sclerodermic patch on the right side of the body, right arm and right side of the hairy part of the head, and also a small area on the left side of the right scapula. Later on there was also noticed atrophy of the right half of the tongue.

Such cases, according to Josephovitch, are of cerebral origin.

Anderson ([92]) has reported a case of scleroderma involving the whole distribution of the right fifth nerve. Alterations were observed not only in the skin, but also in the mucous membranes supplied by the nerve. The right conjunctiva was distinctly affected, and the mucous membrane lining the mouth and upper part of the pharynx was altered in its character. The hair fell out on the same side as high as the middle of the vertex.

Sequeira ([93]) reported two cases of morphœa of the fifth nerve. The first was in a girl, aged 7 years, with a strong family history of tuberculosis. The first and second divisions were affected.

The second case was that of a woman, aged 60 years, in whom the first

and second divisions were also affected. She had besides lupus vulgaris of the nose.

Sequiera concludes: (1) Morphœa does not depend on an affection of the peripheral nerves; (2) that it is probably due to a central ganglionic influence; (3) that it acts by vaso-motor or trophic influence.

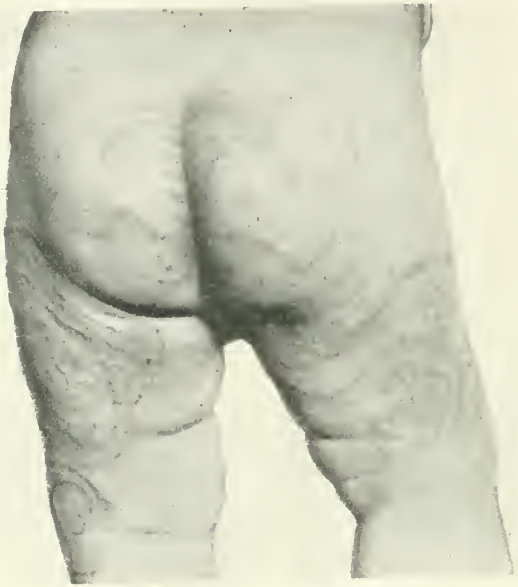
O'Donovan (94) reports the case of a female, aged 25 years, where the first and third divisions were affected. He makes the commentary that this case completes the series needed to support Sequeira's hypothesis of a ganglionic neurotrophic origin. These cases lend support to the hypothesis that the underlying cause is not in the peripheral nerves, but in the Gasserian ganglion.

Steven (95) saw a girl, aged 14 years, in 1886 with a band of morphœa running from the region of the right scapula to the musculo-spiral groove. In 1898 he saw the same patient again. She then had hemiatrophy of the right side of her body, also an ovarian tumour. The tumour was removed and the patient died. Post-mortem it was found that there was slight thinning of the grey matter of the left motor area. Also slight but undoubted diminution in size of the right anterior cornu. The ganglion cells here showed degeneration and were fewer in number. There was no pericardium.

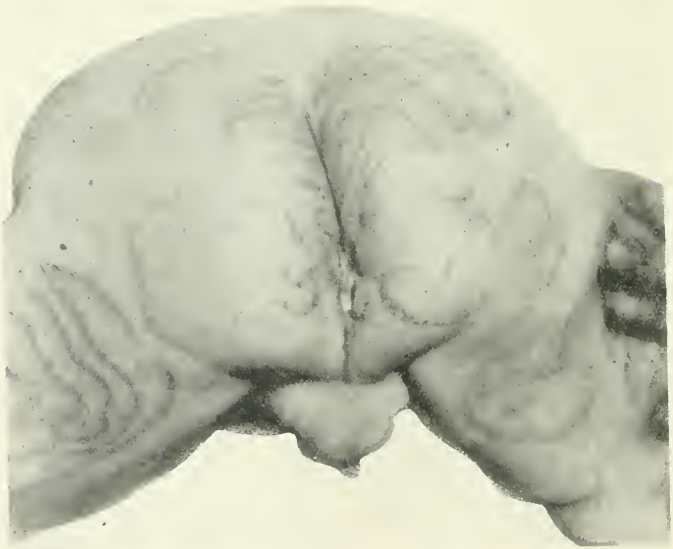
Steven considers the disease is essentially a trophoneurosis, central rather than peripheral.

Thermal.—W. Fox (96) showed a case of morphœa guttata before the Dermatological Section of the Royal Society of Medicine in a woman who had been badly sunburnt. The lesions appeared in the form of a necklet over the sites of the blisters which arose during the sunburning process.

(*To be continued.*)



Congenital syphilitic eruption.



Congenital syphilitic eruption showing anal "mucous patch."

TO ILLUSTRATE DR. WIGLEY'S PAPER ON "AN UNUSUAL RING-SHAPED SYPHILITIC ERUPTION IN AN INFANT."

AN UNUSUAL RING-SHAPED SYPHILITIC ERUPTION IN AN INFANT; WITH PHOTOGRAPHS.

J. E. M. WIGLEY, M.B., M.R.C.P.,
Physician to the Skin Department, Paddington Green Children's Hospital.

Cyril A—, aged 15 months, was first seen by me at Paddington Green Children's Hospital on March 7th. He is the fourth child of the family. The first two children are alive, and said by the mother to be perfectly healthy. The third child was stillborn. This present child was born at full time, apparently perfectly healthy. The ringed eruption was first noticed about one month after birth, has persisted with some variation in intensity of colour ever since, and was regarded by the mother as a birth-mark. About a week previous to being seen a sore was noticed at the anus. It has increased in size, and appears to give the child some pain. The child's general health was said to be good.

When seen, the child appeared healthy and well nourished. A small mucous patch was present at the angle of the mouth, and another larger one at the anal margin. The latter one is well shown in the photograph. The ringed eruption was distributed over both buttocks and the posterior portion of the thighs (*cf.* photograph). The eruption consists of a series of concentric rings, making an irregular pattern somewhat reminiscent of an aeroplane photograph of the trenches. Each line is about $\frac{1}{4}$ in. broad, slightly raised above the surrounding skin, and sharply demarcated from it, of a "raw ham" colour, and covered with a fine scale. On palpation a distinct induration of the lesions can be felt. The skin between the lesions appeared normal.

There was no eruption on any other part of the body. The anterior fontanelle was of normal size, the liver palpable, but not enlarged, and the spleen not palpable.

From the description the lesions have a strong resemblance to those of a case shown by Dr. West before the Clinical Society of London in 1897.

The mother of the child is an anæmic, poorly developed woman, whose mentality is best described as poor. She is also deaf. She can give no history of rash, sore throat, or sores elsewhere. She states that her husband is healthy.

The Wassermann reaction of both mother and child is strongly positive.

Unfortunately the progress of the case could not be watched, as the mother has refused to bring the child to the hospital again.

Reference.

West, Samuel.—"Remarkable Ring-shaped Iris-formed Syphilitic Eruption on the Face of an Infant," *Trans. Clin. Soc. London*, February 26th, 1897, xxx, p. 233.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

Meeting held on February 15th, 1923, Dr. H. G. Adamson, President of the Section, in the Chair.

Dr. A. Winkelried Williams showed a *case for diagnosis*. Patient, a schoolboy, aged 13 years. No drug history, no evidence of food poisoning, no history of any suspicious sore anywhere on body for the last twelve months. He was sent back from school three weeks ago with what was thought to be varicella. Three days later was seen by Dr. Le Riche, of Worthing, who at once noted the unusual features of the eruption. It began as a varicella-like eruption on chest and abdomen, where it was now fading and in some places was gone. It spread centrifugally, the last parts attacked being the soles of the feet and palms of the hands, and it was now just beginning to break out on the face and buccal mucosa. The vesicles capped red papules or macules; they dried up in a day or two, leaving a thin scale which peeled off and left a bluish-red papule or macule showing through the diascope a brownish pigmentation. The rash was thickly studded over the whole body, and was slightly purpuric about the axillæ and lower limbs. A week ago there was no palpable enlargement of the lymphatic glands. Yesterday some glands were hard and enlarged.

Dr. A. Whitfield thought it was a case of disease which had not yet received a name, but looked exactly like secondary syphilis. The present case was the fourth instance of the condition he had seen. He agreed it was a toxic condition; one of his own cases had coli bacilluria, and it would be well to ascertain whether other cases suffered in the same way.

Dr. Graham Little said he was at first inclined to regard it as a syphilide; the glands—epitrochlear and others—were much enlarged. But the vesicular origin of the condition was against that diagnosis. The tonsils also were septic, and he regarded the eruption as toxic. He had never before seen its counterpart.

Dr. J. H. Sequeira referred to the case of a girl, aged 14 years, with a presumably toxic eruption similar to that in the present patient. He was asked to see her during the smallpox scare, as she was living in a crowded boarding-house. She had no temperature when he saw her, but he understood it rose afterwards. It cleared up under symptomatic treatment in a fortnight. She had some glandular enlargement.

Dr. A. Castellani said he had seen a similar condition in the tropics; it was depicted in a plate in the work on *Tropical Medicine* by Dr. Chalmers and himself (see p. 2249). The cases he saw in Colombo were severe. There was a generalised eruption of large papules, which were of bright red colour. Sometimes the cases were mistaken for secondary syphilis, or, in Ceylon, for smallpox. Several glands were enlarged in the tropical cases.

Dr. Semon suggested that the condition now shown might be an aberrant type of pityriasis rosea; the glandular enlargement would support that view; and on the arms, in places, there were the typical scaly rings.

P.S.—Since the meeting a Wassermann test had been done; it was negative. A differential blood-count showed no abnormality.

Dr. E. G. Graham Little showed a case of *urticaria pigmentosa in an adult*. Patient, a girl, aged 20 years, who gave the history that she began to have an itchy eruption in the same positions as the present rash two years ago. She had now a scattered eruption of brownish-red macules on the forearms, buttocks and legs, which became slightly turgid on friction, but did not itch much. A section was taken at another hospital, where she had been under treatment with X-ray applications for some time, with no promising result as regards the lesions. The nature of the section could not be ascertained.

Dr. M. G. Hannay said he had a patient, a man, with a similar eruption; there was definite pigmentation, and an urticarial reaction to scratching. A biopsy, however, showed no increase of mast-cells. The man was aged 36, and he had had the eruption about six years.

Dr. Haldin Davis showed a case of *psoriasis of anomalous type*. Eighteen months ago the patient damaged the middle toe of his right foot,

and a scaly patch appeared on it. Then the nails, first those near the injured toe, and afterwards those more remote from it, became affected. Later the finger-nails were involved. He had also had scaly patches on his head. There were two areas in the groins which, on account of their position, had kept soft, and were not very typical in appearance.

Did the members agree with his diagnosis of psoriasis, and could they suggest any more effective treatment than small doses of X rays? He had tried this both on hands and feet, but without much result; the fingers appeared to be better at one time, but then they relapsed to the former state. The best he was able to do was to keep the nails soft with emollient paste. Ringworm of the nails had been suggested, but no fungus could be found on repeated examination.

Dr. S. E. Dore asked on what grounds the diagnosis of psoriasis was made in this case. He saw this patient privately some time ago, and examined the nails for ringworm, but could not find the fungus. He did not think there had been psoriasis on any other part of this patient's body, or that the appearance of the nails was that of psoriasis.

Dr. Leslie Roberts said he had recently seen a case of psoriasis in which the lesions on the soles of the feet had been modified by pressure resulting from the falling of the plantar arch. The patient's weight was between 11 st. and 12 st., and he had been for the most part confined to the house for three and a half years. The increased pressure had modified the external aspect of the disease, so that the diagnosis of dermatitis had been made. This unusual feature was simply an exaggeration of the intracuticular leucocytosis, which occurred, probably, more or less, in every case of psoriasis. Dr. Davis's case was in some respects similar to his.

Dr. H. G. Adamson (President) said he would not hesitate to regard this as ordinary psoriasis. There was the typical pitting of the nails, and typical psoriasis patches on the groin and scalp.

Dr. J. M. H. MacLeod showed a case of *urticaria pigmentosa*. In this particular case the eruption appeared first as the usual pinkish urticarial lesions when the child was 3 months old. He had brought the case in order to ascertain the view of the members with regard to the ætiology of the disease, which seemed to him to be more of an urticarial than nævoid condition, and was possibly the result of sensitiveness to some foreign protein.

Dr. Graham Little said he deprecated the identification of urticaria pigmentosa with nævus chiefly on the ground that pigmentation was a very essential part of the lesion of urticaria pigmentosa. Urticaria pigmentosa certainly tended to disappear spontaneously, which was certainly not the experience with

any form of pigmented nævi. As regards the fact of disappearance of typical urticaria pigmentosa, he had had an opportunity of establishing this in a case which he saw and recorded in 1908, and had seen again recently. The eruption, a very extensive one, had entirely gone. As regards the diagnosis of cases as urticaria pigmentosa, especially in the adult, he was sceptical of the statement that true instances of this condition occurred with an absence of mast-cells in sections. He had personally never seen such a case, and had examined very many sections derived from numerous cases in both adults and children.

Dr. J. A. Drake showed a case of *urticaria pigmentosa*. This was a case of typical urticaria pigmentosa in a baby. It showed very well the turgescence of the lesions when irritated by clothing or movements ; the condition was extremely irritable.

Dr. J. L. Bunch showed a case of *Boeck's sarcoid*. Patient, a woman, aged 35 years, had a large number of nodules on her face, varying in size from that of a millet-seed to that of a pea. They were irregularly scattered on the cheeks, chin, forehead, and round the orbits. They were of a pinkish or slightly yellowish tint, definitely raised above the surface, firm to the touch, but two or three showed a slight tendency to pustulation, and, on their being pricked, a minute drop of pus could be exuded from them. The section under the microscope showed numerous giant-cells and there was small-celled infiltration. Although the disease was usually described as the sarcoid of Boeck and was said to be related to bovine tuberculosis, he regarded its distinction from acne agminata and acnitis as rather problematical.

The lesions first appeared on the chin nine months ago, and when he first saw the patient the nodules were larger here than elsewhere. As could be seen to-day the chin nodules had practically disappeared, only some scarring being left. This was the result of zinc ionisation, and he proposed to treat the other nodules by the same means. He tried X rays in repeated doses before resorting to ionisation, but the nodules were quite refractory to X rays.

Dr. Graham Little had little doubt that this was a case of acne agminata with all the marks of the group as described by Crocker, the multiplication of lesions in the sulci about the nose, the small translucent papule with little necrosis being especially characteristic. This condition was to be distinguished from acute miliary lupus, which was a much rarer affection, associated with true bacillary tubercle.

Dr. A. M. H. Gray said that some years ago he went into the literature of this subject, and it was very difficult to come to a conclusion as to whether the cases

originally described by Barthélemy as acnitis were the same thing as Crocker's acne agminata; he thought they were not. He did not doubt, however, that the condition Crocker described was the same as the miliary sarcoid of Boeck. Looking at the description of the original acnitis cases, pustulation was a marked feature, while in acne agminata, pustulation, if it occurred at all, was quite a secondary phenomenon, probably due to blocking of infected pilo-sebaceous follicles. It struck him that probably the original acnitis cases were true tuberculides, whereas the cases such as the present one belonged to a different class altogether. The most remarkable point about Boeck's sarcoids was the absence of any tendency to break down; and if one examined sections histologically there was an extraordinary absence of endothelial proliferation. Had Dr. Bunch tried salvarsan injections for this condition? Boeck's sarcoids disappeared in a striking manner under salvarsan.

Dr. J. L. Bunch showed a case of *trichorrhexis nodosa*. All the hair of this girl had broken off at practically the same length; in fact one would have said, from the appearance, that her hair had been "bobbed." She had also nearly lost her eyebrows, *i. e.* the hair had broken off short. A further point was, the mother said that unless the head was thoroughly washed at least three times a week, all the head hair became so matted together and arranged in bundles that the school authorities would not admit her to school. Strong soda and soaps, such as "Sunlight" soap, had been used to try to get rid of the obvious pediculosis, and might have had something to do with the hair becoming brittle and breaking off short, but the trichorrhexis nodosa had been present a long time—for years—and the pediculosis was, almost certainly, of recent origin, or it would have been attended to by the school authorities.

Dr. Knowsley Sibley said he had under his care at the present time a similar case in a single woman, aged 36 years. She had had the disease for three years, and the majority of her hairs showed typical trichorrhexis nodosa structure under the microscope, and her hair, especially over the occipital region, broke off at about half an inch long. He had tried every kind of antiseptic lotion without result. He then gave her a full pastille dose of X rays over the occipital region, and removed all the hairs by the roots, but the new hair which grew showed the same structure. At present she was being treated with ultra-violet rays, and there seemed to be some improvement. Recently she brought her sister, who was 2 years older than she and whose hairs presented the same trichorrhexis condition under the microscope. She had noticed this complaint coming on for about a year. The sisters lived in the same house but did not sleep in the same room, nor even did they use the same brush or comb.

Dr. Arthur Whitfield showed a *case for diagnosis*. This child was first brought to the out-patient department when a few weeks old and

the condition as then seen was in all probability congenital. At that time the salient features of the case were as follows: the child was very puny and small, but otherwise no evidence of ill-health was obtained. The cheeks were swollen, tense, and of a bright vermilion red, with a polished surface. In the centre of the red area on the right cheek there was an oval white patch. On pressure the colour disappeared to a great extent, and revealed the fact that there was a certain amount of nævoid telangiectasis underlying the diffuse redness. The hands were intensely cyanotic and slightly swollen, but at that time no nævoid growth could be detected. Practically the whole of the gluteal region was in the same condition as that noted on the cheeks. The feet were not affected.

Owing to the cyanosis and general condition he had administered small doses of thyroid gland, and during the period succeeding the administration a marked change had taken place. The cyanosis had disappeared and the general condition of the child had improved. The cheeks had lost the swelling and tension, but as the result a nævoid condition had become more evident. The hands had ceased to be blue, but now showed a nævoid condition which had extended up the wrists and was apparently dying down slightly, leaving some pigmentation. The buttocks had undergone the same changes as those in the face, and the feet and ankles had become affected and their condition now resembled that of the hands and wrists.

There had been some nasal discharge at one time, but a careful examination by an expert rhinologist had revealed nothing beyond slight catarrh, and this disappeared so quickly that it was thought to be nothing but a common cold.

He had never seen a similar case, and when he consulted the literature he wondered whether this was an anomalous case of "erythrœdema" or the "pink disease." On the whole he thought not, and was more inclined to view it as a unique case, and was also inclined to think that the symptoms would eventually die away.

Dr. Arthur Whitfield showed an *acarus from case of mange in the human being infected by a dog*. Members were all probably familiar with mange in the human being caught from the dog. Owing to the kindness of Prof. Hobday he had seen an unusually large number of such cases, but in all his experience, and after hours of hunting, he could not find the acarus. Six months ago a practitioner came to see him suffering

from a condition which he diagnosed as mange. The doctor admitted he had a dog, but said it did not scratch very much, and as the doctor gave a history of food poisoning he thought he was wrong. A week or two later the doctor wrote that his wife was affected, and that the dog was scratching. The lady then came to him bringing the dog with her, and the acarus was demonstrated in abundance from the scales on the dog. After a long search he also found a burrow on the wrist of the lady, and picked out the acarus from it.

The other day a lady came to him with a very definite history. She bought a dog from a breeder, and it was covered with mange, and shortly afterwards she developed the typical disease and the daughter developed it too. It quickly died out in the daughter. This patient had the typical mange aspect: that was an erythemato-papular rash all over the body, and everywhere it was intensely pruritic, but there were no runs. He was just giving up the search, when at the tip of one elbow he found a follicle with a slightly brownish speck and it proved to be an acarus, which he had brought for comparison with a human acarus. He was unable to distinguish between the two except by size.

The dimensions of the human acarus were accurately measured, and proved to be 0·33 mm. in length and 0·306 mm. in width. Those of the *Sarcoptes canis* were 0·288 mm. in length and 0·255 mm. in width. That was, the human acarus was larger than that of the dog, roughly in the proportion of 5 to 4—a difference which would render it difficult to distinguish between the two without measurement.

The lesion by which he made the diagnosis was this: if one could imagine a varicella lesion divided by about ten in size, it would be exactly like a mange lesion, *i. e.* a very fine oval erythema, in the centre of which is the smallest vesicle discernible with the naked eye—smaller than a pin-head. He thought probably that the acarus commonly crept into the neck of the hair-follicle. According to the statement in books, if untreated the disease died out in six weeks.

Dr. Wilfrid Fox said these cases were commoner than many supposed. He had recently seen a case which he traced directly to a dog which had ordinary parasitic mange, and which had infected both husband and wife: the lesions were of the type so accurately described by Dr. Whitfield. From the point of view of treatment he did not think it mattered which variety of acarus it was.

Prof. Hobday congratulated Dr. Whitfield on having found the parasite in this case. Being engaged in canine practice, he saw twenty or thirty cases a year in which people were definitely infected from the dog. Quite recently he

had had two cases in medical men. He did not think it was as well known as it ought to be that mange in the dog was responsible for a large number of cases of irritation of the skin in human beings where dogs were kept as intimate pets. In Yorkshire a medical officer of health bought a pug dog which had mange badly, and it contaminated all the members of the family before the source of the trouble was recognised. The front of the forearm, where the skin was very thin, was a common site of infection, and dogs were often allowed to rest on the forearm when being nursed.

Dr. A. M. H. Gray asked whether Dr. Whitfield had ever succeeded in getting the larva of the human acarus out of the papule of human scabies. He (Dr. Gray) had once managed to remove a larval acarus out of a follicle which was at some distance from the main run. He believed that the ordinary urticarial eruption of scabies was due to the larvæ getting into the hair-follicle and setting up irritation in that site.

Dr. Whitfield (in reply) said that he had never found the larvæ. He tried on several occasions some years ago without success, but after seeing this case he might succeed better. Only once had he picked out a male acarus. Unlike the sluggish female acarus, this darted about quite quickly in a drop of water under the microscope.

Dr. J. H. Sequeira showed two cases of *angiomatous granuloma* (*multiple idiopathic pigment sarcoma of Kaposi*). Case 1.—S. F—, tailor, aged 56 years, whom he showed originally in 1913, an account of his case being published in that year.* The patient, of Hebrew extraction, was born in Poland, coming to live in the East End of London in 1905. The illness began in 1911 with purplish swelling of the feet, and when seen in 1913 the left wrist and hand were affected. There was considerable non-pitting infiltration of the skin, which was so dense that the movement of the toes was impaired. In addition to the general purplish infiltration there were discrete papules of similar colour outside the general infiltrated area. The Wassermann reaction was negative. Dr. Turnbull, in an exhaustive report on the microscopical appearances (*loc. cit.*), showed that the chief abnormality was an increase in the number of the capillaries, this increase apparently being due to an actual proliferation, and not merely to a congestion rendering the capillaries more conspicuous. Round and between the capillaries there was a slight proliferation of spindle fibroblasts and a slight infiltration by mononuclear basophil cells. The majority of those cells appeared to be free endothelial cells, a few resembling lymphocytes. There were no leucocytes and no plasma-cells. In another case reported upon by Dr. Turnbull there was much intra- and extra-cellular pigment giving the iron reaction.

* *Brit. Journ. Derm.*, xxv, p. 351.

the deposit of pigment being doubtless a secondary phenomenon due to hæmorrhages from engorged capillaries.

The patient, who still showed the purplish swelling of the extremities, had been under the exhibitor's care for nine years, and from time to time raised flat purplish swellings had been observed on the general infiltration. He had had occasional treatments by X rays, and these had materially diminished the swelling and had thereby relieved the stiffness and occasional pain. The patient's general health had not suffered. He was still well-nourished, though anæmic. There had been no evidence of gout.

Case 2.—D. S—, tailor, aged 61 years, was admitted to the London Hospital on February 7th, 1923. He was of Hebrew extraction and was born in Poland. At the age of 16 he came to London and had lived in the East End for forty-five years.

Two years ago the fingers of the left hand became swollen and he found difficulty in moving them in the morning. The swelling spread to the dorsum of the hand, and to the palmar aspect of the fingers. The swollen areas became purplish in colour. A year ago a similar condition appeared in the right hand and on both feet. On both hands and feet there were numerous irregularly shaped raised purplish areas with sharply defined margins. On the dorsum of the hands there were isolated flat papular lesions in addition to the confluent irregular areas. The fingers were swollen and purplish in colour and the movements were impaired. On the feet the affected areas were mainly on the dorsum, especially along the margins. They were definitely infiltrated, of a dark purplish brown colour with sharply defined slightly raised edges. The toes were not affected. The general health was good, and there were no physical signs of visceral disease. The Wassermann reaction was positive, but there had been no improvement under syphilitic treatment. The blood-count showed no abnormality, and blood-cultures proved sterile. There was no history or evidence of gout.

Histologically the lesions had the same characters as those described above; there were the same increase in the capillaries and cellular infiltration with considerable deposit of pigment giving the iron reaction.

The condition was obviously not sarcoma, and he had long held the opinion that Kaposi's name, "multiple idiopathic pigment sarcoma," should be dropped. As Prof. Turnbull had pointed out, the affection was an angiomatous granuloma, and he (the exhibitor) suggested that this

would be a convenient descriptive appellation to use until the ætiology of this rare affection was worked out.

Dr. A. M. H. Gray showed a case of *so-called Kaposi's multiple idiopathic pigment sarcoma.* Patient, a male, aged 67 years. The lesions appeared suddenly in 1915; he had a few similar lesions on the arms at the same time, but they had disappeared. The affection was not so marked as in Dr. Sequeira's cases, and the case was more doubtful in type. He thought it closely resembled the cases described by the late Dr. Pringle* not long ago. They differed from the ordinary simple hæmorrhagic lesions associated with chronic vascular stasis, in that the lesions were more or less persistent, very sharply defined, and, certainly microscopically, they showed the same type of change which Dr. Sequeira had described. He had a section of one of these lesions, and it showed an extraordinarily sharply marked swelling immediately underneath the epidermis, and slightly stretching it, the swelling consisting of a mass of new connective-tissue cells, and a large number of capillary vessels closely resembling an angioma.

Dr. J. H. Sequeira agreed that Dr. Gray's case was a rather doubtful one. In all the cases in which he (Dr. Sequeira) had been able to make a firm diagnosis the four extremities had been definitely affected, and that affection all began in the intense purple congestion.

Dr. A. M. H. Gray showed a case of *rodent ulcer under treatment with arsenic paste.* Patient, a woman, aged 46, had a nodule in front of her right ear seven years ago. It was first treated with X rays until it disappeared. It recurred, and was treated at Norwich Hospital with X rays and CO_2 snow for eighteen months; it was also scraped several times. Subsequently it received about a year's treatment with X Rays at Lowestoft Hospital. He (Dr. Gray) first saw her in April last, and the size of the ulcer then was shown by this photograph (exhibited). He had brought her to show how he used the arsenic paste in dealing with these extensive ulcers. The area was first scraped very thoroughly, and in certain cases portions of the growing edge were excised. The paste, which was suggested to him by Sir Norman Walker, and which consisted of arsenious anhydride 1 part, sulphide of mercury 5 parts and animal charcoal 1 part mixed with a little spirit immediately before

* *Proceedings*, 1918, xi (Sect. Derm.), p. 107; 1919, xii (Sect. Derm.), p. 48.

application, was then applied in a thin layer over the scraped area. In this case as the area was so extensive it was treated in two parts, the anterior half being dealt with first. There had been two local recurrences calling for further applications of the paste, but the whole area now appeared to be quiescent. There was a large area of bare bone, practically the whole temporal fossa was exposed, and the zygoma had already separated. The rest of the bone would separate in due course, but it often took many months.

Dr. O'Donovan said that treatment of rodent ulcer by arsenic paste had largely gone out of use, and it was interesting to see a form of treatment in which the old generation of surgeons had had confidence. The only alternative treatment for advanced cases of this type was an extensive surgical removal, and a successful result even then could not be predicated.

Dr. A. H. M. Gray showed a case of *erythema of face following an injection of N.A.B.* The patient, a female, aged 27 years, developed secondary syphilis, and on January 12th last he gave her a first injection, 0·45 grm. of N.A.B. intravenously. The same evening she became feverish, and in twenty-four hours had developed a curious rash on her face. It had now practically gone. The rash consisted of a butterfly patch on the face, a patch in the centre of the chin and patches on the sides of the neck, and a V-shaped patch in the suprasternal region. The patches stood out sharply from the skin, and were very œdematous. The temperature for several days was 104° F., and gradually subsided. She had had fairly severe albuminuria since the injection, 6 per cent. by Esbach's method, and it had not yet entirely gone. She was said to have had acute erysipelas of the face three months before, which kept her in bed for two or three weeks, but she had no fever.

He thought that both these attacks were acute lupus erythematosus, and that the disturbance caused by the injection of N.A.B. was responsible for bringing out the second attack. He had never seen any description of such a condition following a salvarsan injection.

Dr. H. G. Adamson showed a case of *recurrent cellulitis*. Patient, a young woman, aged 23 years, had had recurrent attacks of cellulitis of the face during the past two years. The cellulitis involved both lips and adjacent parts of the cheek, the gums and anterior part of the hard palate. At each attack there was swelling of these parts with redness

and tension of the skin, the redness and swelling showing a sharp margin as in an attack of erysipelas. At first these attacks occurred every two or three weeks, but the intervals had increased, and now they occurred only every few months. The swelling had never completely subsided between the attacks, so that there remained a gradually increasing thickening of the lips and cheeks until the patient now presented a "leonine" aspect. The patient had been examined from time to time in the throat and nose department and in the dental department, but nothing had been discovered which might be suspected as the source of origin of the complaint. There were no nasal fissures and no fissure in the lip.

Such cases were not uncommon, and he brought this case as an example, with a view to discussing the point of origin and the treatment of these cases. In his own experience no treatment had been of any avail in this complaint, except perhaps repeated doses of X rays, which had seemed to him to diminish the frequency of the attacks. He had tried streptococcal vaccines, intravenous injections of collosol copper and intramuscular injections of collosol manganese without any good result. Although he suspected these cases to be of the nature of recurrent erysipelas, Dr. Mervyn Gordon, who had examined many cases for him by deep puncture, had in no case been able to obtain a culture of streptococcus, so that it had not been possible to give an autogenous vaccine.

Dr. H. G. Adamson showed several cases of *lupus vulgaris* treated by liquid acid nitrate of mercury.

Dr. O'Donovan said he had made an extensive trial of acid nitrate of mercury in severe cases of lupus of the skin of the nose—cases wholly unsuitable for Finsen light; his results had been most gratifying. The scars of Dr. Adamson's cases were beautifully smooth and supple, and in an extensive scar below the right eye the absence of ectropion was remarkable.

Dr. H. W. Barber showed a case of ? *pemycosic erythrodermia*.

Dr. J. L. Bunch showed a case of *adenoma sebaceum* in a girl, aged 10 years.

MANCHESTER DERMATOLOGICAL SOCIETY.

Meeting held on March 9th, 1923, Dr. G. H. Lancashire, President, in the Chair.

Dr. Gibson showed a case of *recurrent erythema multiforme* in which the lesions were some of them bullous in type and some papular. The back of the neck, dorsa of hands and forearm were the chief areas involved; the mouth was not affected.

Dr. Savatard offered a *case for diagnosis*. A young boy showed a large number of cysts and papules along the upper and lower eyelids. These appeared last August, and were followed in a week or two by several similar lesions along the right side of the neck; the former treated by X-ray and improved, the latter disappeared spontaneously.

Dr. Lancashire showed a case of *tertiary syphilis* in a middle-aged woman. The lesions were very superficial and slightly indurated; the edge was serpiginous and gave a clue to the diagnosis.

The interesting feature was the close simulation both in distribution and appearance to lupus erythematosus. Early scarring was to be seen in the centre of the lesions.

Dr. Savatard showed a young boy with *lymphangiomata*. The tumours were on the side of the neck; they were like red currants in size and colour and were confined to an area in the posterior triangle of the neck. They were firm but compressible, and varied slightly in colour from a very pale red to a deeper colour.

Dr. Lancashire showed a case of *multiple basal cell carcinomata*, which had been previously shown prior to treatment. This consisted of erasion, resorcin dressings and intense X-ray therapy. The many previously affected areas showed healthy pliable and flat scars.

Meeting held on April 6th, 1923, Dr. G. H. Lancashire, President, in the Chair.

Dr. Dyson showed (1) *a case of acnitis*. The patient was a young adult male in whom the outbreak occurred about 10 weeks ago; all the lesions had appeared during the course of a week. The eruption consisted of red papulo-nodular lesions varying in size from a pinhead to a pea,

scattered evenly over the cheeks, brow, and upper lip. They were rather closely grouped, however, along each eyebrow. Some of them showed a small pustular tip, but when pressed were found to contain no purulent material. By diascopy they had a jelly-like appearance closely resembling a follicular lupus.

Microscopic section showed granulomatous masses, some of which appeared to have been infected; they were not confined to the follicles. Some of the follicles had involuted, leaving small depressed scars.

Dr. SAVATARD read Dr. Brookes' monograph on "Varus Nodulous," and pointed out that the condition was identical.

(2) *Case for diagnosis.* A boy of 12 years had developed purpuric lesions along each arm at intervals of about 3 months during the last 2 years. The skin on the first examination had been markedly urticarial; the hæmorrhage had the appearance of having developed, along scratch-marks. The patient stated that he had very little itching during the development of the lesions, or at any other period. He stated that they appeared after rubbing.

On the day of examination the skin was only slightly urticarial, no definite wheals appearing. The boy had bruised very easily since a baby, but had never shown any other hæmophilic tendency. The exhibitor suggested that the diagnosis was that of traumatic lesions in a mildly hæmophilic patient.

Dr. SAVATARD showed two cases of *epithelioma adenoides cysticum*, which had been shown before the Society and which had been treated by X-rays and expression of cyst contents. The cases showed a very marked improvement in appearance. The exhibitor made a point of the frequent invasion of the upper lip in these cases, which serves as a point of differentiation from adenoma sebaceum of the non-Pringle type, and demonstrated an excellent case of the latter affection of the Pringle type. The tumours were telangiectatic, and closely and evenly spread over the nose and cheeks in large numbers. The patient stated that they were quite painless, and beyond their readiness to bleed were no trouble. Sections of this case were shown.

Dr. PROSSER WHITE showed the following *case for diagnosis*. A nurse, 30 years of age, who suffered from patchy baldness. She stated that her hair had been slowly falling out from scattered irregular areas of her

head for the last 12 years. On examination many such atrophic colourless patches were found; they were scarred and slightly depressed. There was no sign or history of inflammation and the direction of the spread was irregular. There was no dilatation of blood-vessels; there were no stumps present, but from several of the scarred areas healthy hairs were seen to grow. The case was suggested to be one of cicatricial alopecia (pseudo-pelade).

Dr. Dyson also showed a very severe case of *tubercular disease of the skin* in a young man with marked elephantiasis of the right arm from tuberculous lymphangitis. The axillary glands were tuberculous also, and several bony sinuses were present at the wrist. There was no evidence of intestinal pulmonary disease.

CURRENT LITERATURE.

INFLAMMATIONS, ETC.

A CASE OF TRIPLE ORIENTAL SORE OF THE FACE, TWO OF WHICH WERE PROBABLY LYMPHATIC METASTASES. P. Stancanelli. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1923, fasc. i, p. 37.)

The case reported was in a man, aged 20 years, who developed a Delhi boil on the centre of the forehead, and later two other lesions appeared symmetrically in each zygomatic area. The author emphasises the fact that these sores are single in the majority of cases, and if multiple are usually due to successive inoculations. If the lesion confers a specific immunity, it appears very slowly. In cases of multiple sores, especially if they appear in the vicinity of the primary, one is possibly dealing with metastases. In such a case the metastases probably spread by the lymphatics, and frequently infect either the lymph-glands or points of convergence of lymphatic vessels where there is a slowing of the circulation.

R. C. L.

A CONTRIBUTION TO THE STUDY OF THE VEGETATING STAPHYLOCOCCAL DERMATITES. M. Artom. (*Giorn. Ital. d. Mal. Ven. e della Pella*, 1923, fasc. i, p. 43.)

The lesion was a chronic warty one with swelling on the right side of the face of a man, aged 33 years. The Wassermann reaction was negative, as also the tuberculin Pirquet reaction. Search was also made for various fungi but none were found. Microscopically the swelling consisted chiefly of leucocytes and some epithelioid and plasma cells. No giant cells were present. *Staphylococcus pyogenes aureus* was obtained in pure culture from the lesion. Artom considered the lesion as a granuloma due to the staphylococcus. The case was cured by injection of an autogenous vaccine.

R. C. L.

THE PATHOGENESIS AND TREATMENT OF SCLERODERMIA. V. Ramazzotti. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1923, fasc. i, p. 51.)

A case of typical sclerodermia is described in a man, aged 61 years. Within six months the head, face, neck, trunk and limbs were affected with a sclerodermia, which interfered considerably with movement. After considering the different theories as to the cause of sclerodermia, the author determined to treat him with X-rays to the different organs supposed to be implicated in the causation. First the rays were applied to the hypogastric region on alternate days for four times to see the local effect on the skin. The treated area improved somewhat. A second series of rayings was giving with the object of altering the endocrine secretion. The thyroid gland, testicles and suprarenals were exposed to the rays. This resulted in a slight softening of the skin on the buttocks, but otherwise the condition was unaltered. A third series of rayings were given to the cervical, dorsal and lumbar areas of the spine. This caused a marked and progressive improvement in the skin condition, and gradually the whole condition cleared up and disappeared. R. C. L.

LUPUS ERYTHEMATOSUS ACUTUS D'EMBLÉE. J. W. van der Valk. (*Acta Dermato-Venereologica*, iii, 1–2, p. 63.)

Case report of a recently married young woman, aged 23 years. Admitted to hospital with the diagnosis of erysipelas, the patient showed the affection on the face, hands and feet, including the rare involvement of the soles. On the trunk was an eruption which could not be distinguished from lichen scrofulosorum. Generalised adenitis. The v. Pirquet reaction was positive and Wassermann reaction weakly positive on admission, to become negative. Broncho-pneumonia and nephritis. The case was treated with cacodylate of soda and recovered. In the author's opinion these cases were probably not so rare as the literature would suggest, some of them being probably regarded as erysipelas if the skin manifestations formed the chief feature of the disease, while those cases with uræmia and pneumonia were seldom seen by dermatologists. All the four cases of this disease which he had met had been accompanied by marked pediculosis capitis, and there might be some association, direct or indirect, between these two conditions. W. J. O.

ERYTHEMA EXSUDATIVUM MULTIFORME (HEBRA): SOME CLINICAL OBSERVATIONS. Brünauer. (*Arch. f. Derm. u. Syph.*, 1923, cxlii, 2, p. 195.)

The relations between cutaneous and mucous membrane eruptions in this disease are by no means constant, in that either may proceed as an initiatory manifestation.

In this article the author describes four cases in which the characteristic lesions appeared on the glans penis—a site not hitherto reported since Hebra's classical description of the disease.

The individual appearances consisted of a superficial loss of epithelium, of rounded outline, the base of the ulcer covered with slimy discharge, and the ulcers surrounded by a ring of active hyperæmic reaction. Here and there were seen the relics of the dried roof of a vesicle or bulla, showing the original nature to have been of that character. Typical painful manifestation of erythema multiforme

were present on the skin of upper and lower extremities, and fever was also noted in all the four cases.

[The penile lesions appear to have presented the same features as those not uncommonly met with in the mouth.—Transl.]

Treatment by oral administration of salol and peroxide irrigation resulted in complete involution in about 3 weeks. H. C. S.

PATHOLOGY.

ON THE GENESIS OF MELANIN BY BENZO-PIRROL. Mario Quattrini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1923, fasc. i. p. 20.)

By injecting pirroll, α-carbo-pirrollic acid, α-methyl-indol and skatol subcutaneously, Quattrini produced a local pigmentation of the skin in animals. In suitable animals (rabbits) this leads to the production of brownish areas arranged in lines, reticular form, isolated spots or diffuse areas, when the pigmentation is intense and rapidly produced. The pigmentation usually appeared between the ninth and eighteenth days, and sometimes earlier with α-methyl-indol. The extent of diffusion of the pigmentation varied with the substance injected, beginning with α-methyl-indol, which gave the least diffusion, then α-carbo-pirrollic acid, then skatol, and lastly pirrol, which gave the greatest diffusion. Skatol produced the most intense pigmentation. The rapidity of appearance, extent and intensity of the pigmentation are not proportionate to the quantity injected. The best results were obtained by using 0·19 cgrm. of α-carbo-pirrollic acid in fourteen days, 0·36 cgrm. α-dimethyl-indol in nine days and 0·33 cgrm. skatol in nine days (always per milligramme weight of animal). Larger or smaller doses gave inferior results. Pigmentation was never produced in the skin of albino animals nor on the white areas of animals with white and coloured areas of skin. In coloured guinea-pigs the production of pigmentation appeared in approximately the same time as in rabbits, although the phenomena were less apparent and slower in being established. The hair re-grew more rapidly and strongly on the pigmented area and had the colour and appearance of the long and not of the downy hairs. Analogous phenomena were also seen in albino animals although with complete absence of pigmentation. The intensity of coloration was greatest at the proximal part of the hair and diminished towards the tip, but always maintained a more intense colour than normal.

These substances never caused local reactions of any importance with the exception of a slight swelling, and in one case of a circumscribed gangrene. All had a general effect, skatol being the most toxic and α-methyl-indol the least so.

The pigmentation persisted up to fifty-four days, with a constant tendency, especially in the first month, to extend over the whole dorsal area of the animal, even on to areas where the hair had not been cut. The pigment accumulated exclusively in the hair, and in lesser quantity in the sheath of the hair and in the apex of the hair papilla. It consisted of black granules inside the cells to such an extent as to obscure the structure of the cell.

The pigment was found by the seventeenth day in the circulation and in the internal organs (spleen, liver, kidney). In the spleen it occurred as yellow-brown or greenish masses which had been phagocyted by macrophages. In the other

two organs it occurred in lesser quantity in the form of black granules in the liver-cells and in the cells of the renal tubules and intertubular connective-tissue cells.

The article is illustrated by coloured drawings of the pigmentation in the hairs and internal organs, and also by photographs of the animals.

R. C. L.

EXPERIMENTS ON THE SUSCEPTIBILITY OF HUMAN SKIN TO ANIMAL SERA. Biberstein and Oschinsky. (*Arch. f. Derm. u. Syph.*, March, 1923, cxlii, 3, p. 353.)

The human material selected for these investigations were individuals of both sexes, and from 20–35 years of age. Susceptibility to light and recognised sensitivity to proteins excluded not a few of them, and the subjects were all, as far as could be ascertained, normal in their skin reactions. All injections were given intracutaneously, and the sera were obtained from three sources, viz. rabbit, sheep and guinea-pig.

The paper is unusually long and technical, and it is only possible here to give an abstract of the conclusions reached.

(1) Normal human skin reacts variously on first injection to the three sera tested, *i.e.* the primary susceptibility varies. Moreover, there are individual differences to the same serum. The development of local reaction after an incubation period of 7–8 days, after one injection only, may be regarded as a local example of "serum disease."

(2) Re-injection of the same serum after 5–7 days was followed uniformly by the specific allergic reaction, and could be obtained up to 3 weeks from the date of the first injection. After 4 months reactions were negative to the original serum, but repetition a week later produced positive results in 3 hours only, thus proving a raised proclivity to antibody production brought about by the original injection more than 4 months previously.

(3) Sensitisation can be effected by subcutaneous to intracutaneous injections, and *vice versâ*.

(4) Individual immunity, in the sense of a lack of reactile sensitivity, was not found in any of the forty-six normal persons investigated.

In syphilitic subjects, however, there were a large percentage of negative or relatively immune results.

Two cases, previously treated by casein injections intramuscularly, responded *unspecifically* positive in their reactions.

(5) Very minute doses ($\frac{1}{10}$ of ·1 c.c.) of serum were able to produce specific reactions in previously sensitised skins. Non-specific anaphylotoxin (Nathan) elicited no local reaction.

(6) Biological and clinical incubation times for these reactions are by no means identical. This is evidenced by the fact that a positive Wassermann reaction in syphilis is frequently obtainable long before the appearance of the disease in the skin or mucous membranes. The authors believe that with improvement in modern technique it will be possible one day to show that the biological incubation period is infinitely small, and practically contemporaneous with the moment of primary infection. H. C. S.

TREATMENT.

USE OF THE ESSENTIAL OIL OF TURPENTINE IN THE TREATMENT OF SKIN AND VENEREAL DISEASES. L. Mazzini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1922, fasc. vi, p. 1165.)

The author found oil of turpentine very efficacious in the treatment of pyogenic dermatoses, suppurative ringworms, and adenitis of venereal soft sores. The injections are easily carried out and free of risk, whether given intramuscularly or intravenously. The intravenous method is no better as regards rapidity of action than the intramuscular, which is slightly painful. The author considers this method of treatment preferable to protein therapy as it does not produce such intense general reactions. R. C. L.

RÖNTGEN-RADIUM TREATMENT OF PSORIASIS. C. Guarini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1923, fasc. i, p. 65.)

The author treated recent cases of psoriasis with X-rays in doses not greater than 2 H. with a filter of 1–2 mm. of aluminium giving a total dose of 6 H. in each series of exposures. In the chronic inveterate cases he gave exposures of 5–6 H. with a filter of 3–4 mm. of aluminium, the whole dose in each series totalling 15–18 H. He used a hard tube, raying wide areas at a time. By these means he states he obtained very good results. He also used the method recommended by Brock for young persons. Brock showed the persistence of the thymus gland in psoriatics and treated cases by X-raying the thymus gland, giving small stimulating doses. The author treated fifteen cases by this method and reports very good results in all except one. Recurrences are rare after this method. The author mentions the treatment of psoriasis with radium, but quotes no cases.

The author (who is a radiologist) claims that X-ray therapy is to be preferred to other forms of treatment in the majority of cases when it is carefully applied by a skilled operator. He states that in his department ointments have been to a great extent discarded in favour of X-rays, and that in treating psoriasis the radiologist and the dermatologist should collaborate. R. C. L.

THE INCREASE OF THE FUNCTION OF THYMUS BY X-RAYS AND ITS INFLUENCE ON THE SKIN. Karel Gawalowski. (*Česká Dermatologie*, 1923, iv, p. 94.)

In the treatment of psoriasis by X-rays the author obtained successful results in 65·8 per cent. of cases. He used a somewhat larger dose and shorter intervals than Brock. The clinical course of healing was analogous to that under local treatment by X-rays, the difference being one of subjective nature; a severe itching developed in a week and lasted three to four weeks. Increased tendency to pigmentation was noticed under this treatment (patients tan more easily). In some cases (with fresh papules) eight to ten days after irradiation of the thymus pustules developed on the psoriatic areas. This phenomenon may be explained by the fact that, under the influence of fresh thymus hormone, parakeratosis begins to disappear and the cocci in the layers of the skin are no longer removed mechanically by desquamation; the microscopical epidermal abscesses (Haslund) have a chance to develop into larger pustules. Pustules were not noticed in cases treated by local irradiation. It seems that thymus does not increase the

formation of defensive forces in the skin. Recurrences also seem frequent under Brock's method. Everything considered, this method is a valuable antipsoriatic measure; on account of anatomical and physiologic conditions it is, however, rather uncertain. SPINKA (St. Louis).

CARBON DIOXIDE SNOW THERAPY. PAVEL BEUTL. (*Ceská Dermatologie*, 1922, iv, p. 1.)

PUSEY's carbon dioxide snow treatment has been tried with good results at the skin clinic in Brünn. The lesions of the face were especially benefited by this method. Freezing alone has been used in cases of simple vascular and pigmented nævi, lupus erythematosus, keloids and cases of epithelioma. Several cases treated by combined methods are reported. An extensive verrucous linear nævus was previously treated by Unna's digestive fluid to remove the horny masses; in a hemifacial cavernous hæmangioma the external maxillary artery was ligated and freezing then combined with electro-cautery: nine cases of epithelioma were exposed to Röntgen rays a day after freezing (two recurrences). In lupus vulgaris (ninety-two cases) the tubercles were at first disintegrated by means of Finsen light or by electro-cautery, and then freezing was used to bring on a more rapid resorption of newly formed pathological tissue and a better scar. In lupus vulgaris of the face the author favours the combination of freezing with the sodium chloride method as used by Jadassohn.

SPINKA (St. Louis).

SYPHILIS, ETC.

LEUCODERMA SYPHILITICUM. S. EHRMANN and L. WERTHEIM. (*Arch. f. Derm. u. Syph.*, April, 1923, cxliii, sect. 1–2, p. 128.)

IN this detailed clinical experimental study the authors availed themselves of the pigment-stimulating effects of the ultra-violet rays on the skins of luetic patients. The lamp was applied in each case at a distance of 30 cm. for ten minutes. The article is illustrated with some striking photographs. The conclusions are as follows:

For the production of leucoderma syphiliticum there should be—(1) a demonstrable preceding alteration of the skin, *i. e.* either a macular or maculopapular eruption; (2) the skin on which it is desired to produce the phenomena of leucoderma must itself be pigmented to start with.

The leucoderma may be evoked before an eruption is evident, during its evolution or subsequently, by external stimulation, *e. g.* light, as long as the luetic cell damage lasts. There are cases, however, in which both these postulates are fulfilled and yet no leucoderma results. A third and unknown factor, possibly of central nervous origin, may be requisite, but appears doubtful to the authors.

Disappearance of the leucoderma occurs either when—(1) the hyperpigmentation is absorbed and equalisation results; (2) when strong stimulation results in the absorption of the pigment into the depigmented areas; or (3) neither process takes place, and equalisation is the result of recovery of pigment-forming cells. H. C. S.

A COMPLETE OBSTRUCTION OF BRONCHUS CAUSED BY A GUMMATOUS PROCESS. P. Svoboda. (*Ceská Dermatologie*, 1922, iv, p. 15.)

Report of a case of complete obstruction of left bronchus 1 cm. below the bifurcation of the trachea. No air was entering the left lung, the patient suffering from extreme dyspnœa. He also showed an undermined ulcer with lardaceous base on the right shoulder. Administration of potassium iodide resulted in a complete cure. Spinka (St. Louis).

NEW CLINICAL REACTION OF SYPHILITIC MACULES. Samberger. (*Ceská Dermatologie*, 1923, iv, p. 89.)

Luetic macules appear in greater numbers and become much more pronounced when the patient is instructed to stand up and bend over several times. Spirochætes reduce the vitality of blood capillaries. A macule is the mildest clinical expression of the resultant decreased function—a passive hyperæmia. The latter becomes more marked when some extra work—like the above exercise—is thrown upon the weakened venous capillary system. Analogous results are obtained in cases of cutis marmorata. Spinka (St. Louis).

CONTRIBUTION TOWARD THE STANDARDISATION OF BORDET-WASSERMANN REACTION. J. Kabelik. (*Ceská Dermatologie*, 1922, iv, p. 68.)

This is a technical article describing the author's modification of the reaction and reasons for same. Spinka (St.Louis).

SALVARSAN. J. Crha. (*Ceská Dermatologie*, 1922, iv, p. 74.)

In a review of clinical experiences with salvarsan and neosalvarsan, the author favours intramuscular injections of neosalvarsan according to Balzer's formula ("Glueo 914" and "Harsol.") Intramuscular injections show the same effect on the clinical symptoms and Wassermann reaction as the intravenous medications. The technique is simple. The complications are less frequent. With a careful dosage the injections are well tolerated by the aged and by patients with internal complications. Spinka (St. Louis).

BISMUTH—THE NEW ANTILUETIC REMEDY. Victor Sedlak. (*Ceská Dermatologie*, 1922, iv, p. 10.)

At the clinic in Bratislav, "Trépol," the tartrobismuthate of potassium and sodium in oil suspension, has been given a trial. Seventy-six cases of lues in various stages were treated. A course consisted of ten to twelve intragluteal injections: First two of 2 c.c. each two days apart, then three 3-c.c. doses three days apart, final doses five to six days apart as the infiltrate becomes slower to disappear. The drug seems well tolerated. Gingivitis often appears, but never was it so bad as to interrupt the course of treatment. The lesions promptly disappeared. In some cases—mucous lesions and late manifestations—the healing was more rapid than ever noticed under salvarsan or mercury. In its direct spirochæticidal effect the bismuth is superior to mercury but inferior to salvarsan. Spinka (St. Louis).

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THE ENDOCRINE CAUSATION OF SCLERODERMA, INCLUDING MORPHŒA.

W. F. CASTLE, D.S.C., B.A., M.B., B.Ch.(Cantab.).

(*Continued from p.* 278.)

The following twelve cases were personally observed, and I am indebted to Dr. Sequeirâ and to Dr. Semon for permission to publish some account of them.

Case 1.—Winifred W—, aged 11½ years, attended the Out-Patient Department at the Royal Northern Hospital for four years and was finally discharged in June, 1922.

She was born in England and was of English parentage. She suffered as a small child from measles, whooping-cough (which lasted for four and a half months) and influenza. Her health otherwise had always been good, but she was inclined to outgrow her strength. She was of nervous temperament, but was not irritable. Her family history presented nothing of importance. There was no tuberculosis in the family.

In 1917 her mother noticed a small patch on her daughter's face, starting at the inner canthus of the left eye and spreading out on to the left cheek. It was white and shining, and gradually increased in size until it covered most of the left cheek.

In 1919 the white patch near the inner canthus cleared up.

In 1920 the child was taken to the seaside and at the end of her stay was very sunburnt. The pigmentation spread on to the affected part of the face, and although the child is now pale and of clear complexion, the pigmentation has remained in the sclerodermic patch.

In June, 1922, the condition was as follows: The child was of good physique. The heart and lungs appeared normal. The urine contained neither sugar nor albumen; its reaction was acid and its specific gravity 1018. The nervous system seemed normal. The abdomen was normal, except that the girl complained of pains in the stomach after exercise. The tonsils were small and looked healthy. There was no evidence of any thyroid disease. There were no enlarged glands. The hair was normal and showed no tendency to fall. There

was severe dental decay. The blood-pressure was 90 systolic and the pulse regular at 110. The Wassermann reaction was negative. The skin was moist and healthy except on the left side of her face, where it was atrophied, wrinkled and pigmented. There seemed to be some atrophy of the left malar bone, but this was not shown by the X-rays. The jaw was symmetrical, also the forehead. The lesion was entirely limited to portions of the first and second divisions of the fifth cranial nerve. The palate was normal. All the cranial nerves except the fifth were normal. The disease appeared now to be stationary.

The treatment adopted was the administration of thyroid extract for three months. This did not seem to influence the disease in any way and so was discontinued. There had never been any symptoms of thyroid disorder.

The special features of this case were :

(1) The pigmentation of the affected areas, possibly caused by the sun's rays.

(2) The fifth nerve was affected, which seems to occur in an unduly large proportion of cases.

(3) The spontaneous cessation of the disease.

Case 2.—Mary G—, aged 54 years. London Hospital. Housework. This patient came for consultation on account of the appearance round her neck of numerous patches, varying in size from a pin's head to a two-and-sixpenny piece. The patches took the form of a necklet round the base of her neck. The spots were of a dead white colour with a slightly raised edge which was faintly lavender-coloured. There was considerable itching over the affected area. The spots had appeared gradually during the past two years.

The patient was married and had two children who were alive and well. Her husband had died of pneumonia. Her family history showed nothing abnormal. She had suffered from the usual children's illnesses, she believed, but she had never had any serious disease. Change of life had occurred at 48 with no untoward symptoms.

Examination of the patient showed that her heart was normal. Her pulse was regular (78) and was of good tension. Her blood-pressure was 140 mm. of Hg. (systolic). Lungs were normal. Her nervous system was normal. Her abdomen was normal. The Wassermann reaction was negative. Her urine was acid, contained no albumen or sugar, and its specific gravity was 1014. The thyroid was not enlarged nor were there any symptoms of thyroid disorder. She was a healthy-looking and well-formed woman. Dental sepsis was present to a considerable degree.

She was treated with extract of thyroid and massage, but failed to attend and has been lost sight of. She had shown no improvement.

The appearance of a collar of spots is fairly common, and is so striking to the eye that it has caused a great deal of attention to be focussed on this form of scleroderma, especially in America, where a vast amount of literature has accumulated on the subject.

Case 3.—Amy A—, aged 32 years : housework (1922). Came to the London

Hospital for advice for the skin on her shoulders. She had noticed a feeling of lumpiness, which had been increasing for the last fourteen days.

In 1913 she had suffered from gastric ulcer and had been in the London Hospital under Lord Dawson. Since then she has always suffered from indigestion on the slightest indiscretion. At 17 she used to be very anæmic. She had had no other illnesses. Her menstruation had started at the age of 14, and had always been regular but painful until her child was born in 1918. She had to have instruments, as the labour was prolonged.

Her family history was as follows: Her father died at the age of 52 from cerebral hæmorrhage. Her mother died at 65 from aneurysm and heart failure. Four sisters were alive and well. One brother was now well, but at the age of 8 years had had his leg amputated for tuberculosis of the ankle.

Her present trouble started as far as she knew about a month ago, when she noticed that the skin between her shoulders had a feeling of lumpiness. She thought that during the past 14 days the lumpiness had increased.

Examination showed two patches of morphœa: (1) Of a butterfly type, $6\frac{1}{4}$ in. between the tips of the wings and 4 in. deep, at the base of the neck, more to the right side than to the left; (2) a patch $3\frac{1}{2}$ in. by $1\frac{1}{4}$ in. over the right scapula.

These patches were hard, of an ivory colour, with one or two hard black plugs at the opening of the sebaceous glands.

She also complained of a bad circulation in her fingers, which she said became numb in the early morning. During the past winter she suffered from chilblains and the skin of her hands became rough and cracked. All her fingers tended to "go white," especially at their tips. This had never happened before 1921. Her fingers, when seen on a very hot day, showed no signs of this bad circulation of which the patient complained. The general clinical examination showed that her heart, lungs, urinary and nervous systems were normal. Her teeth were in good condition. Her heart was regular and free of adventitious sounds. Her pulse was 70, regular, and her blood-pressure was 120 mm. of Hg. Her Wassermann reaction was negative. Her urine was acid, contained no albumen or sugar, and its specific gravity was 1012.

Her skin appeared normal except for the two patches of morphœa. Her hair was not falling out. She stated that she had no sexual feeling, and that connection was most distasteful. She tired easily and Sergent's sign was easily elicited. There were no signs of thyroid disorder. She had never suffered from flushes. She stated that she liked the cold weather very much, and that except for her hands she always felt warm.

She was ordered massage, and extract of thyroid gr. j *t.d.s.*, with no improvement up to the present (four months later).

The association of scleroderma with either a real Raynaud or a modified form of the disease, as in this case, is very common, and has been commented on by many authors, especially by Hutchinson. There were no definite signs of endocrine deficiency, with the possible exception of the sexual glands. The adrenalin insufficiency, as shown by Sergent's sign, and the general weariness, was not marked, nor can this sign and symptom be taken as definite proof of deficiency.

Case 4 (1922).—F. M—, aged 25 years, a Russian Jewess. First attended the Out-Patient Department at the London Hospital in March, 1921, for post-partum debility.

When she was three months pregnant she noticed that her hands and legs were swelling. Thinking this to be merely a condition connected with her pregnancy she did not seek advice. This condition persisted throughout her pregnancy which terminated at seven months, and afterwards. The child was healthy and the labour an easy one.

Family history.—Came to England when aged 2 years; she was born in Poland. Both her parents are in England and are in good health. Her mother is a hunchback. There is no skin disease in the family.

Past history.—No previous illness of note. Two children alive and well, (1) aged 4 years, (2) aged 9 months.

When first seen in the Out-Patient Department she was of pale complexion with some pigmentation of her body. There was a fulness of her face and a doubtful right-sided facial paralysis. She had a slight swelling of her arms; her legs were normal. Her appetite was poor, her bowels opened regularly, her tongue was clean and moist, and her teeth were good. Her heart, lungs and abdomen presented nothing abnormal. Her urine was acid, specific gravity 1023, no albumen or sugar.

She was diagnosed as Raynaud's disease and given massage and baths. Her condition did not improve, and on May 3rd, 1921, the baths were stopped, and alternating currents were substituted with no better results.

In November, 1921, she was sent to the skin department, and on December 15th, 1921, she was admitted to hospital.

Condition on admission.—There was a leathery condition of the skin of her arms and legs with loss of elasticity and adhesion to subjacent tissues, the condition spreading gradually from the extremities. There was some loss of movement at the wrist, elbow, ankle- and knee-joints. Above the elbows and knees the skin appeared to be normal. On the toes there were some corns present, some of which had ulcerated. The knuckles and tips of the elbows were in the same condition, owing to the stretching and inelasticity of the skin. The face was smooth and without wrinkles, the expression being mask-like. The skin condition was spreading on to the neck. She could close her eyelids, but could not screw up her eyes tightly.

Three weeks later examination showed.—Hands: Flexed at first and second phalangeal joints and kept so. There was ulceration of the skin on the extensor surface of the first joints, with the formation there of septic thickenings of the skin. *Right elbow* could bend from 90 degrees to 60 degrees. There was a shallow ulcer ·5 cm. in diameter over the tip of the olecranon process. *Face:* Sallow, earthen colour; the skin was very shiny, tightly drawn and smooth, all wrinkles being obliterated. There was no epiphora or ectropion. Teeth easily shown. Eyelids opened and shut easily. The skin over the front of her chest and less so over her shoulders was inelastic, smooth and moist. There was no loss of sensation. The movement of both shoulders was free and not painful, but was little used owing to much pain in moving her elbows. *Knees* were permanently flexed at 160 degrees, but could easily be bent to a right angle. *Ankles* were stiff. Arches of feet exaggerated. *Thighs, legs and feet* felt hard to

the touch. The skin was rigid, indurated and resistant. There was no œdema. Hair was present. *Toes* could be flexed and extended a little. They were cold and blue. Crepitus could be felt by pressure on the patella when the knee was flexed.

After a month more in hospital, with regular massage and thyroid gr. ½ twice daily, there was considerable improvement. She felt better, the skin seemed more supple and the septic pressure sores all healed. She was more cheerful, could talk more easily and move about the bed with less difficulty. Her face seemed fatter, and she showed more expression when talking and smiling. There was a certain amount of dental sepsis. Her temperature was between 98 and 99 degrees during this period, and her pulse averaged 100. There was nothing abnormal in her nervous system. Examination of cerebro-spinal fluid showed:

Clear fluid.
3·5 cells per cubic mm.
Type = small lymphocytes.
Protein was present in slight excess.
Wasserman reaction was negative.

The blood-cound was as follows:

Red cells	5,660,000 per cubic mm.
Hæmoglobin	85
Colour index	·79
Leucocytes	6400
Polynuclear neutrophils	61·5 per cent.
Polynuclear eosinophils	1·0 ,,
Small lymphocytes	23·5 ,,
Large lymphocytes	6·0 ,,
Large hyaline cells	7·5 ,,
Coarsely granular basophils	0·5 ,,
	100·0 ,,

The Wassermann reaction in the blood was negative.

X-ray examination showed:

(1) Sella turcica to be normal.

(2) A general thinning of the bones of the knees, feet and hands.

A portion of the skin was removed, divided after fixation into three segments, and reported on by Prof. Turnbull:

"(1) (2) (3) *Scleroderma diffusa from skin of left elbow.* There is no appreciable difference between the three segments. The skin contains hairs, arrectores pilorum, sebaceous glands and sweat-glands. The segments, unfortunately, only include a few fragments of subcutaneous tissue. The most striking abnormality is the heavy pigmentation of the basal cells of the epidermis. Similarly pigmented cells are abundant about the vessels in the outer part of the dermis. The pigment does not give the Prussian blue reaction of free iron, and is doubtless melanin. The papillæ are as well developed as in controls. The bundles of collagenous fibres of the dermis, both in the papillary and reticular zones, appear to be stouter than in six controls; this appearance was confirmed by actual measurements. In most places the bundles are set more closely together than in the controls. The elastic fibrils are normal in number and distribution. There is

a perivascular infiltration, which varies in amount and is never great. Mention has already been made of the numerous cells loaded with melanin round the vessels of the papillary and outer reticular zones. The majority of the other cells in the perivascular infiltration here, and in the remainder of the dermis, are mast-cells; plasma-cells are also present, and, in places, especially in the central and deeper portions of the dermis, are numerous. Mast-cells are also present round the hair-follicles; about one or two hair-follicles there is an infiltration comparable to that round the vessels. There appears to be no infiltration about the sweat-ducts and glands, apart from that about the vessels which are associated with them. The vessels are in part collapsed, in part filled with red corpuscles. There is no endarteritis. The material examined does not suffice to justify an attempt to interpret the pathological process."

On February 8th, 1922, as the pulse-rate was gradually creeping up and as the patient was not feeling so well the thyroid extract was stopped. On February 16th three minims of a 1 in a 1000 solution of adrenalin were injected subcutaneously; the blood-pressure rose in three minutes from 90 mm. Hg. to 100. Four hours later it had risen to 175, and four hours later still it had fallen to 160. Four days later it was again 90. This reaction, together with the bronzing, seeming to indicate the possibility of adrenal insufficiency, it was decided to try the experiment of grafting adrenal substance into the patient as soon as a suitable occasion presented itself. This, unfortunately, was delayed until the first week in May, and by that time the patient had wasted very considerably. The pigmentation also had become very pronounced all over her body.

On May 4th there were two stillbirths in the hospital, one from a placenta prævia, and the other from a prolapse of the cord. Between four and five hours afterwards Mr. Walton operated.

Operation.—Upper left rectus incision. Spleen brought into the wound and its capsule incised, and several small pieces of suprarenal were inserted. These were retained in position by sutures. The liver capsule was incised, and several pieces of supra-renal were embedded in liver substance. The wound in the liver was closed with catgut. Several small pieces were inserted under the skin on either side of the upper left rectus incision. The wound was closed in layers. The suprarenal was removed from the stillbirths.

After the operation the patient was extremely collapsed, and for forty-eight hours it was very doubtful if she would recover from the shock. However, she rallied, and on May 12th her blood-pressure was found to be 85 (systolic).

Pigmentation of the skin of the face seemed to be fading quite appreciably.

May 13th: Blood-pressure—systolic 90, diastolic 80.

May 16: Blood-pressure 90. Doing well.

May 18th and 20th: Blood-pressure 90. The patient was put on a couch, but complained of feeling very tired.

May 22nd: Blood-pressure 85.

May 25th: Blood-pressure 100.

May 27th: Blood-pressure 95. Patient seems less tired on being put on a couch. Pigmentation very much less on the face. The skin condition does not seem to have altered to any extent.

June 20th: The blood-pressure has remained steady at 90 systolic. The

bronzing of the face and hands has quite disappeared, although the body is still as dark as before the operation. Bed-sores have appeared at the points of pressure, the subcutaneous fat having been completely absorbed.

July 10th: There has been no change at all in the patient.

August 2nd: The patient was discharged from hospital as her condition appeared to be stationary.

This case, which was something of an experiment, bears out the general findings which a trial of adrenalin has led us to expect; here, however, the adrenals were grafted into the patient, in the hope of obtaining a more prolonged action than is possible with the administration of the gland extract. Also it was hoped that the grafts would grow as there appeared to be an urgent need of adrenalin, and as it has been shown that a graft is much more likely to grow if there is a decided call for it in the patient into whom it is placed.

The weakness, bronzing and low blood-pressure which were present in this case all seemed to indicate adrenal deficiency, but, just as in Addison's disease, it seemed impossible to try to supplement the adrenalin supply; probably injections of adrenalin are useless as they are oxydised in the body tissues immediately.

Case 5.—Gertrude H—, aged 27 years, was admitted to the London Hospital on June 15th, 1920.

History.—Six years ago she noticed a small white patch with lilac edges which suddenly appeared on the right side of the base of her neck. This had been preceded for some months by a general itching, which kept her awake at nights. About this time also her hair fell out in bunches.

The original patch spread and others appeared on the left side of her chest. When she was first seen she had four patches (two large and two small) on the left side of her chest. There were none elsewhere. The patches spread slowly towards the mammary region. After this the lesions remained almost stationary.

In January, 1916, there was still very little change except for a few spots on her legs, but a further spread of spots, which started about November, 1919, brought her up to hospital. Itching on the chest and arms had been constant at nights, but not severe. Since the age of 15 she had had a lump in her neck (in the thyroid region), which became larger when she was menstruating, and she thought it used to make her talk thickly. In January, 1915, the lump enlarged considerably. Her doctor gave her thyroid to take. She suffered at times from general flushing, her hands shook, and she was low-spirited and irritable. No eye signs were observed then. She always perspired freely and passed a lot of water. In January, 1916, she was given a dose of X-rays to her thyroid (Sab. ½ per 1 mm. filter). This made no noticeable difference, but in 1919 the swelling was less appreciable, although her tremors and irritability were still present.

Family history.—Her mother and father are alive and in good health, although her mother suffers from kidney disease. One brother and two sisters are alive and well: one sister died in infancy. She has been married for four years, and has one child, aged 2 years. There have been no miscarriages. She suffered from measles and scarlet fever when she was a child. She has never been very strong, and can only manage her housework with difficulty. Her catamenia is very painful, but is regular.

On examination (1920): The patient was a rather delicate-looking woman; she seems very highly strung. Flushed readily on being spoken to.

Skin.—There were many smooth, irregular, ivory patches with lilac margins, up to the size of a five-shilling piece, scattered over the front of her chest and sides, the right side of her back over her lower ribs, her axillæ, right arm and the upper part of both thighs, and all over her abdomen. The patches in the axillæ were seen to sweat. Elsewhere the skin was supple and moist. Her hair was soft and scanty.

Nervous system.—Tremors of the hands were well marked. The patient was irritable and easily frightened. The pupils were equal and reacted to light and accommodation. There were no eye signs present, such as are usually found in hyperthyroidism. Knee-jerks obtained easily. *Tâche cerebrale* easily elicited.

Heart.—The apex-beat was just outside the nipple line in the fifth space; there was a soft systolic murmur heard in all areas. Her pulse ranged between 84 and 104 and was regular. Blood-pressure was 110 systolic.

Abdomen and chest appeared normal. Her temperature was normal. Her urinary and digestive systems were normal. Her thyroid was uniformly enlarged; no thrill or bruit was perceived. Her Wassermann reaction was negative.

She was given general treatment and injections of enesol (salicylate of arsenic and mercury), but the local reaction was so great that they had to be discontinued. She made no improvement, and was discharged *in statu quo.*

So many cases are now on record of disease of the thyroid together with scleroderma that a large literature has sprung up on the subject. The treatment of scleroderma by thyroid extract is presumably based upon these cases. Sweating of sclerodermic patches is contrary to experience and does not bear out Crocker's experiments with the injection of pilocarpine, when he found that the skin round the patch sweated, but that the patch itself remained dry. This case was one of myxœdema which, with the administration of thyroid extract, showed signs of hyperthyroidism.

Case 6 (1921).—Ada D—, a Russian Jewess, aged 38 years. This patient came to the London Hospital complaining of white spots on her neck. She had first noticed them one month previously. She stated that she knew when fresh spots would appear, as she suffered from itching over the site of the new place for about a week previous to the appearance of the spot.

When seen she had a complete collar of spots round the base of her neck. The spots varied in size from a pin-point to a threepenny-piece. The spots in places seemed to coalesce.

Family history.—Mother and father both dead, but the cause was not known. She had three brothers and a sister who were alive and well. The patient was married and had had seven children, the youngest of whom was a year and a half old. They were all in good health.

Past history.—Always had good health.

Examination of the patient showed a prematurely old, well-nourished woman. Her neck showed the lesions described above. The skin on the rest of her body was dry and harsh. She said she did not sweat at all. Her hair had been falling out for the past two months and had been becoming grey since the age of 32. Her heart was normal, her pulse regular, rate 60, her blood-pressure 140 mm of Hg. Her nervous system was normal except that her reaction time was delayed. Her lungs, digestive and urinary systems appeared normal. Her thyroid gland could not be felt. Her gums and teeth were in a very bad condition.

When seen in January, 1922, the collar of spots had spread widely on to the front of her chest and the upper parts of her breasts. She was given thyroid extract gr. j *bis die* for four months, as well as daily massage, apparently without any benefit to her spots or to the general condition of her skin. When last seen the disease was progressing posteriorly and all the surface of the mammæ was sclerodermic.

This was a fairly well-defined case of myxœdema with morphœa, and was a good example to compare with Case 5, both cases having disease of the thyroid—one hyperthyroidism, and the other hypothyroidism.

It was certainly surprising that this case did not improve in general condition with the administration of thyroid extract.

Case 7 (1921).—Alice M—, aged 35 years. This patient came to the London Hospital complaining of two white patches on her back. She said that she had first noticed them twelve months previously, and that they were spreading slowly.

Family history.—Father died at 58 of kidney disease. Her mother was well. No brothers or sisters. This patient was married, and had had two children. The first one died three days after birth from "paralysis"; the other one was healthy. The spots started when she was nursing.

Past history.—No illness which she could remember, but she always suffered from indigestion, which had, however, disappeared after the birth of her last child.

On examination the patient appeared to look healthy, but was very nervous. *Skin:* Her back showed two patches, circular in outline, with dark pigmentation at the periphery—(1) over the left posterior clavicular region; (2) over the left scapula. Both patches seemed hard to the touch, and were of a yellowish-ivory tint. The skin on them was wrinkled, and there were several black horny plugs which seemed to be the opening of the sebaceous glands. These plugs could be squeezed out. The remainder of the skin appeared to be normal. Her hair was said to be falling out rapidly.

Examination of her lungs, abdomen and urinary systems showed them to be normal. Her nervous system was normal, except for her unusual nervousness. Her mouth was clean. Her heart was normal, her pulse regular, and was at the

rate of 60 to the minute. Her blood-pressure was 130 mm. of Hg. Menstruation normal. Wassermann negative.

She was treated with thyroid extract and daily massage, but up to the present there has been no improvement. The disease appears to be stationary.

Lactation and pregnancy have often been quoted as being associated with the start of scleroderma, but when one considers the very small number of cases relatively, it seems very unlikely that this is anything more than pure chance.

Case 9.—Maud S—, aged 17 years, domestic servant, was admitted into the London Hospital on May 5th, 1922, suffering from scleroderma and hemiatrophy of the right side of the face and tongue. Her illness dated from August, 1920, when she noticed the appearance of white patches on her right breast and arm. These patches were quite painless and she knew of no possible cause for them. In 1921 she noticed that the right side of her face and her right breast were wasting.

Past history.—She had always been healthy and had had no previous illnesses.

Family history.—Contained nothing of importance.

On examination the patient appeared to be a well-grown, well-nourished girl. Her right breast, the right side of her face and the right side of her tongue were smaller than the left. The skin on her face was shiny and atrophic on the right side. The bones of the affected area seemed to be much smaller than those on the left side. The skin of the neck was normal. The left side of the tongue was considerably larger than the right side. The right breast was small and atrophic the nipple was normal. The left breast was plump and healthy.

There seemed to be no paralysis of the affected muscles, merely atrophy. There was a patch of scleroderma about the size of a shilling just above the right nipple and two others on the extensor surface of the right arm. There was a hard lump the size of a walnut in the right axilla which was thought to be either an inflamed gland or a fibroma. The right side of her neck seemed smaller than the left side. There was doubtful wasting of the right side of her hard and soft palates. There was no pigmentation. Swallowing was easy. There was no adenitis except possibly the lump in the right axilla. There was no excess of salivation. Voluntary power of the limbs, co-ordination and sensation were normal. Eye movements were normal, also the fundi. Menstruation started at 14½ and was apparently normal.

The heart was normal and regular in rhythm. The pulse ranged between 70 and 100. Blood-pressure was 150 systolic, 60 diastolic. The nervous system, lungs, digestive and urinary systems were normal. Her teeth were bad. The Wassermann reaction was negative. X-rays of the right chest and kidney area showed no abnormality.

During her stay of fourteen days in hospital the patient lost four pounds in weight. An injection of 5 minims of adrenalin solution (1/1000) was given subcutaneously with no definite rise of blood-pressure. She was discharged from hospital and told to attend out-patients. She was given ext. thyroid 1 gr. *t.d.s.*

I have not seen her since at out-patients nor has she come up for more

medicine. A photo of the patient at the age of 12 years, which she sent up for inspection, shows no apparent wasting of the right side.

This is an extremely interesting case, as the wasting is considerably greater than in other reported cases, where the hemi-atrophy is usually limited to the face. Whether in this case the wasting was due to some nervous factor, and, if so, whether this was secondary to some endocrine disorder, is not certain, but this latter supposition seems improbable, as in these cases the atrophy is usually bilateral.

Case 10 (1918).—Iris K—, aged 10 years, was admitted to the London Hospital in August, 1916, suffering from sclerodactyly and hyperthyroidism.

Previous history.—In September, 1914, the girl had been very badly frightened and since then she had lost her appetite and become very nervous. She had lost weight and her speech had become nasal. For the past year the skin of both hands was gradually becoming glossy and red, with a gradual contraction of her fingers and thumbs. In 1909 she had scarlet fever, chickenpox and measles. In 1913 she had ringworm of the scalp, which was treated by X-rays.

Family history.—Father and mother and five brothers and sisters all alive and well.

The condition of the patient on admission was as follows: She was a pale, intelligent girl. Her speech was nasal. Her eyes were prominent and there was a doubtful enlargement of her thyroid. There was no tremor; her pulse was 86: night sweats were present; her temperature was normal. The skin over both hands and wrists was very glossy and pigmented; numerous scars were present over the finger-joints; the nails were shiny and brittle and longitudinally ridged; the fingers of both hands were stiff and contracted, and the movements of her fingers were limited. Her feet were cyanosed but there were no contractions. The skin of her scalp was shiny in places. Her Wassermann reaction was negative. She was discharged unimproved and readmitted in September, 1917.

On readmission her condition was as follows: Her face was mask-like in appearance, the skin was shiny and tight; there was a complete absence of wrinkles and creases; the skin appeared to be stretched and could not be raised from the underlying tissues. The child spoke as though she had a mild form of cleft palate. Her hands were flexed at all joints distally to the metacarpo-phalangeal joints; the more distally the joint, the more acutely flexed it was. Movement was greately restricted. The joints of the fingers were slightly swollen, bluish at times, and in many places there were scars and ulcerations. There was wasting of the muscles of the hands. The hands were pigmented; there was a brownish colour which extended half way up the forearm. As far up as the elbow the skin was shiny and appeared stretched; the skin was firmly adherent to the underlying structures.

The skin was more or less affected as far up as the knees, but the discoloration was less marked than on the hands. The feet were of a purplish hue. There were scabs and crusts scattered all over the legs and feet. Nodular swellings, about the size of a small pea, were noted along the tendons of the flexor longus digitorum.

The back and abdomen showed a few scattered scars of herpes zoster on the left side at the level of the eighth and ninth dorsal nerves. The skin elsewhere was normal.

The apex-beat of the heart was 1 in. external to the nipple line in the fourth space. There were no adventitious sounds heard. The lungs were noted as being free from disease. There were no enlarged glands. The tonsils were inflamed and were extensively cavitated. There was chronic inflammation of the left tonsil. The abdomen was healthy. The urine was acid, specific gravity 1025. No albumen or sugar was found. One month after admission there was a sudden rise of temperature to 103° with swelling of the left hand and forearm, due probably to infection of the middle knuckle of the left hand. There was no swelling of the glands. Under treatment with fomentations and lysol baths the condition gradually subsided.

The general treatment given during her stay in hospital included the administration of thyroid extract gr. j three times a day. She was discharged after two months unimproved.

Readmitted into hospital in November, 1918. The skin condition was then noted to be much the same as before. The heart was drawn to the left, the apex-beat being drawn upwards and outwards. There was dulness in front down to the third rib, and over this area the breath-sounds were harsh and almost bronchial. Posteriorly in the left lower scapular region the percussion note was tympanitic and the breath-sounds were very loud and bronchial in character. The only added sounds heard were a few crepitations in the left axilla. The signs seemed to indicate fibrosis of the upper part of the left lung, probably with a cavity nearer the back than the front. X-ray examination indicated fibrosis of the left upper and lower lobes of the lung. The heart was more transverse than normal and was displaced to the left. The liver was enlarged and reached nearly to the iliac crest.

On December 21st the temperature rose to 103·5° and the patient died on December 24th. No post-mortem was allowed.

Tubercle of the lung with possibly disease of the suprarenal as suggested by various authors as a cause for scleroderma is an attractive, but hitherto unproved theory. It is a very great pity that no post-mortem was permitted in this case.

Case 11 (March, 1922).—C. R—, aged 31 years, married, presented herself for treatment with a band of scleroderma which commenced at the tuberosity of the left tibia, spread out over the leg, to end at the internal malleolus. The band was 1¼ in. broad at its upper end, and gradually passed into normal skin. There were no dilated veins or abnormal pigmentation. There were two patches of scleroderma, the size of a shilling, over the internal condyle of the femur. Both areas and the band had suddenly appeared four years previously, and had not altered in appearance or in size. The patient had two children—a boy who suffered from debility, and a girl. The boy was 10 and the girl 8 years old. She had had no miscarriages. Her past illnesses she did not remember, but at school she was considered to be anæmic. Family history showed nothing abnormal. The patient was a well-nourished woman, bright and cheerful.

Her chest, abdomen, urinary and nervous systems were normal. Her teeth were in excellent condition. Her Wassermann reaction was negative. Blood-count 5,600,000 red cells, 8100 white cells. Differential white-cell count was normal.

A section cut of the band on the leg showed increased fibrous tissue and diminished papillæ. Her thyroid was normal to the touch. Her skin was moist and flexible; her hair was in good condition. She felt the cold rather badly and her periods were rather painful.

There has been complete cure after three months' treatment with massage, thyroid and parathyroid extracts.

Case 12 (May, 1922).—A. W—, a boy, aged 8 years, was brought to the London Hospital by his mother because of a patch of hard skin on his chest. This patch was a band of scleroderma, two inches wide, of rectangular shape, running horizontally round the right side of the chest. The area affected was about 2 in. by 6 in. The affected skin was hard and firm, ivory white in colour, with no increase of pigmentation at its edges, but with a few dilated blood-vessels at the periphery, which was somewhat lilac-coloured. The scleroderma had been noticed fourteen days previously. There was no history of any injury or fright.

The family history was normal, mother and father and four other children being alive and healthy. The previous history of the patient included infantile paralysis at the age of 1½ years, which had left him with paralysis of the anterior tibial group of muscles of the right leg. The boy also showed swelling of the cervical glands, which, in the absence of any septic focus, were considered to be tuberculous. He had also suffered from whooping-cough and measles; there was no history of tubercle in the family.

Examination of the patient showed a healthy-looking boy; chest, urinary, digestive and nervous systems were normal. Wassermann reaction negative; differential and total blood-counts were normal. No abnormality of the thyroid could be detected.

Treatment with extr. thyroid gr. ½ *t.d.s.* and massage for two months produced no improvement, and the child ceased to attend.

Conclusion.

Out of the large mass of literature which has appeared on the subject of scleroderma, there is very little indeed which helps to any great extent in the elucidation of its ætiology.

The disease is one that has attracted a great deal of interest in all the civilised countries of the world, as, although cases are so few and far between, they are so striking that they cannot fail to arouse considerable attention.

A fair proportion of this paper has been devoted to those cases of scleroderma which are supposed to have been due to some deficiency of the

internal secretions; in this part will be found statements purporting to show that in a particular case the disease was due to a deficiency of either the thyroid, pituitary, or adrenal glands.

In most of these cases the deductions are founded on a misconception; it is surely erroneous to suppose that because the extract of a gland may improve or even cure a case, the underlying cause of the disease was a deficiency of this gland? But this argument is used over and over again, and very little else is brought forward in support of this supposed endocrine deficiency.

Taking these three sets of cases separately, it appears at once that the thyroid is reported to be at fault in many more instances than the pituitary and adrenals. It must indeed be more than a coincidence that scleroderma is found in such a great number of cases of obvious thyroid disorder. From all the clinics of Europe and America have come reports of cases in which scleroderma has been found in association with either Graves's disease, myxœdema or thyroid tumour; yet so far nothing definite has come to light from which to draw conclusions. The fact that scleroderma can appear in Graves's disease and myxœdema—two totally different diseases—must make one very cautious of making any deductions. The extraordinary report by Dittisheim of eight cases of scleroderma in seventeen consecutive cases of Graves's disease, shows that the association between the two diseases must be something more than mere chance.

There surely must be some close connection between some forms of scleroderma and disease of the thyroid? The two are so often found together and have even been reported to disappear together.

Among the authors who have reported cases connected with pituitary disorder, there are very few who have investigated their cases thoroughly. Little mention is made of estimating the sugar tolerance of the patient, or of taking radiographic pictures of the skull, or of even describing the patient's growth and stature; in some cases one or other of these things has been done, but on the whole these reports are most unsatisfactory.

Schwartz' ([35]) report is of very little value, and it appears that he falls into the very common error of deducing the ætiology from the manner of the cure.

Izar's ([37]) case is undoubtedly a good one, and strongly suggests a pituitary origin for the scleroderma in this case at any rate. One should, however be very cautious in accepting this theory; one case out of the

enormous literature is not sufficient material from which to come to any definite conclusion.

The papers written in favour of the adrenal causation of scleroderma are quite insufficient from which to draw deductions. Probably the pigmentation, which so often occurs in both diseases, is the real reason why some authors believe them to be connected. Addison's disease is associated with the deposition of a pigment in the skin that is generally considered to be a melanin, differing from that normally produced in the skin only in quantity and not in origin. No satisfactory explanation of the relation of the adrenal to this pigment seems yet to have been made, although it seems permissible to assume that when the function of the adrenal is destroyed, substances accumulate in the blood, which have a stimulating effect upon the pigment-forming cells. This explanation is possibly correct in some cases of scleroderma, although examinations of the suprarenals after death do not seem, except on very rare occasions, to have found their way into the literature, and even in these few cases no sections appear to have been cut. A further resemblance between Addison's disease and scleroderma is to be found in the manner of death, which in both cases is often very sudden.

Clinically and pathologically, Addison's disease and scleroderma are different, and it is only in a very few signs and symptoms that they show any likeness to each other.

Ætiologically they are possibly related through an abnormal action of the sympathetic; although proof of this is very difficult, it is quite possible that a sympathetic disorder, together with a derangement of the ductless glands, may be the cause of scleroderma.

If now the other ætiological suggestions be considered, much of considerable interest appears, and possibly a short discussion of the various factors concerned would be of value.

Trauma and *irritation* can be grouped together, and under this heading appear several very interesting cases. It seems improbable that either of these can be the actual exciting cause of the disease; so much trauma occurs daily in all walks of life and so little scleroderma, that a close connection between the two seems scarcely possible. However, it seems probable that damage to the skin and subcutaneous tissue may predispose the subject to scleroderma if there are any other influences present which would by themselves tend to produce scleroderma.

The case recorded under the heading of *thermal* is an excellent example

of this. The morphœic lesions occurred at the sites of the blisters, but it must be asked, how many blisters become sclerodermic, and can this case be more than a coincidence, or did the rays of the sun cause some profound change in the individual ?

Shock has been mentioned in many cases as the exciting cause. There is, it seems, no doubt that fright causes a profound stimulation of the sympathetic nervous system, which was originally a protective system, and if, as many think, scleroderma is intimately connected with the endocrine glands, which in their turn have a very close relationship with the sympathetic, there seems a very strong possibility that shock may be one of the exciting causes of scleroderma. During the past war, however, the combatants were constantly in a state of acute fright and considerable alarm, and yet no increase of scleroderma was noticed ; but, in spite of this in many cases fright and nervousness seem to have been of considerable ætiological importance.

The theory that any *infectious disease* may be followed by scleroderma is not justified in my experience. Nearly all the infective fevers have at one time or another preceded scleroderma, and I can only say that I have had no experience whatever in this association.

The suggestion that scleroderma is closely related to *rheumatism*, and that in both diseases similar blood pictures have been found, together with increase of fibrin in the circulating blood, has not been verified by other laboratory workers, nor does it seem probable that it will be, as rheumatism and heart disease are very closely related, while heart disease is not found in scleroderma, or, if it is, as purely a chance occurrence.

Failure of the *mesenteric glands* as a cause for scleroderma seems improbable, nor has the originator of this theory brought forward any evidence in support of it.

Scleroderma is probably never *congenital*, although it may be noticed shortly after birth ; the so-called congenital cases are probably accounted for by the amniotic bands.

Pregnancy has been shown in many papers to be the time when scleroderma first appeared. In pregnancy a large extra strain is thrown on to a woman, and her ductless glands have to provide for a growing child ; that this extra strain may be too great is readily to be understood, but if pregnancy causes scleroderma in the mother, would it not be likely that the child would suffer from this disease too ? In these reported cases it has not been suggested that any particular ductless gland in the woman

is to blame for the scleroderma, but it is a well-known fact that the thyroid is often found to be swollen and over-active in pregnancy, and it is more than probable that other glands are either over- or under-active at the same time, and so it does not seem at all improbable that pregnancy may have a definite influence on the ætiology of scleroderma.

Syphilis cannot be numbered among the likely causes of scleroderma, as the finding of a positive Wassermann reaction is at present so common that if syphilis had any considerable influence, it is probable that scleroderma would be of much more common occurrence.

The association of *Raynaud's* phenomena in conjunction with scleroderma has been noted in a large number of cases, and it seems most likely that the two diseases may have some common causation.

Herman Goodman ([63]) noticed a very curious fact about scleroderma—that, in a very large proportion of cases, it starts either on the neck, or on the face. This observation is borne out entirely by clinical experience, and it is very difficult to give a satisfactory explanation for it. Goodman suggested that possibly this was due to an affection of the tonsils, spreading through the skin lymphatics, thus supporting the old theory that scleroderma is due to a lymph stasis. This is not now believed to be the correct explanation, but no other is forthcoming.

The theory of a *nervous* origin for scleroderma has more supporters than any other theory. So many cases are now on record where the disease has been limited to particular nerve areas, especially the trigeminal, that a nervous origin seems more than likely. Again, many cases show complete symmetry of the lesions, and in some there is a complete hemiatrophy with muscular wasting, and no alteration of the sensations of the affected parts. These cases certainly strongly support the idea of a neurotic basis for the disease. Whether, as some think, scleroderma is due to a tropho-neurosis of central ganglionic origin, or, as others think, to an affection of the cutaneous branches, is still a matter of doubt; nor is it evident what is the cause of the nervous origin, but there is a strong possibility that it is due to some failure of the endocrine glands.

Analysis of the 12 cases which I have personally watched shows that eleven occurred in females and 1 in a male. This is certainly an unusual proportion, as the usual incidence of scleroderma is 1 male to 3 or 4 females. The ages ranged between 8 and 54. In no case was there any clinical or serological evidence of syphilis.

In seven cases the disease was first noticed on the face or at the base of the neck.

No cause could be assigned for the disease in any of the cases, except possibly in Case 10, where a severe fright was held to be responsible.

Two of the twelve cases suffered from tuberculosis, while in two more cases there was a close relationship to tuberculous patients.

Pigmentation occurred in four cases.

Disease of the thyroid was found in three cases, in one of which myxœdema developed into hyperthyroidism.

No other evidence of endocrine deficiency was found, except, possibly, in Case 4, where an adrenal deficiency was suspected.

From the consideration of my own, and the many published cases, I consider that the essential cause of scleroderma is a combination of a disordered function of the internal secretory glands, together with an affection of the nervous system. It is more than probable that the internal secretory system acts as a whole, and that if any particular gland fails, the remainder act in a way to minimise that failure, and so it is impossible to fix the responsibility for scleroderma on to any one gland. If the thyroid is enlarged, and there are signs of hyperthyroidism, is it not quite possible that this syndrome is the reaction which is called forth by the failure of one or more of the other endocrine glands in an attempt to minimise the deficiency ?

The cause of the failure of one or more glands in scleroderma cannot in most cases be determined. Severe nervous emotion must undoubtedly be seriously considered as a possible cause owing to its influence on the sympathetic system, which, in its turn, is closely related to the internal secretory glands.

In many cases, however, no history of shock or of prolonged mental strain can be elicited, and in these cases it seems probable that the underlying cause for the endocrine failure is a long-continued poisoning, either from dental, intestinal, or tonsillar sepsis. The teeth of the average hospital patient are usually in such a bad state that it is difficult to estimate correctly the amount of damage for which dental sepsis may be responsible.

The cases in which there has been long-continued slight trauma, such as those in Bramwell's series, may be accounted for by the trauma taking the place of the endocrine failure and affecting the cutaneous nerves directly.

That an affection of the nervous system is present in scleroderma seems most probable when one considers the many cases in which hemiatrophy is present, and also those cases in which the affection is limited to one or more branches of the trigeminal nerve. Whether this affection is of central ganglionic origin in the form of a tropho-neurosis, or whether it is an affection of the cutaneous branches, still remains to be determined.

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CLINICAL NOTE.

A FATAL CASE OF LUPUS ERYTHEMATOSUS DISSEMINATUS.

W. KNOWSLEY SIBLEY, M.D., and W. H. WYNN, M.D.

An apparently healthy, well-nourished single woman, aged 23 years, was admitted under my care (W. K. S.) into St. John's Hospital for Diseases of the Skin on September 1st, 1921, with a typical superficial butterfly patch on her face, associated with a slight attack of tonsillitis. In a few days some similar lesions appeared on her chest, and shortly afterwards the butterfly patch on her face completely disappeared, to reappear in a more intense form in a fortnight's time, together with an increase of the lesions on her chest, and others appeared on other parts of the trunk. Her general health was good, and she was not inconvenienced by the disseminated rash which had appeared. On December 12th she complained of headache, and her temperature rose to 103° F., remaining about that level until the 15th, when it went up to 105·6°, and pulse to 128. On December 19th the temperature had dropped to 100·4°, when an extensive bulla appeared on the right leg. From this time the temperature varied from normal to 99°, occasionally rising to 100°. The bulla dried up in the course of a few days and did not recur. The patient left the hospital in an ambulance on January 26th,

1922, for her home in the country, and was admitted into the General Hospital, Birmingham, on February 5th, and the following are the notes of her subsequent history (W. H. W.) :

On admission she had a profuse erythematous rash on the face, scalp, arms and legs. On the back it was intensely scarlet. On the abdomen and chest there were large white patches, raised and surrounded by areas of pigmentation. On the soles there were some small ulcers. The right tonsil was very septic and inflamed. On February 9th the rash faded somewhat, but she had a rigor and the temperature went up to 106°, and the next day there was intense œdematous swelling of the face and neck. Leucocyte count 27,000. A pure culture of streptococcus was found in the blood.

10 c.c. antistreptococcus serum was given on the 10th, 11th and 12th; this was followed by improvement. On the 15th, 5 millions autogenous streptococcic vaccine was given and again on the 18th, and $7\frac{1}{2}$ millions on the 21st. She appeared to be going on very well. On the 18th it was noted that she felt very well; the rash had faded and was replaced by desquamating areas. There was no redness anywhere. On the 23rd the temperature again rose, and on the 27th reached 106·7°. The rash again returned, but was rather different—a yellowish diffuse rash on the arms and large patches on the legs. The legs became very swollen and moist with much weeping. Serum and vaccine were again given, and she began to improve. Notes on March 2nd, 6th and 8th say that she was feeling much better. With the exception of the swollen, discharging legs the rest of the rash had faded. It was thought that she was going to get well, but on the 9th the pulse became irregular, she had difficulty in swallowing, and had sighing respiration. She died on the morning of the 10th.

The urine contained albumen, granular casts, pus-cells and streptococci.

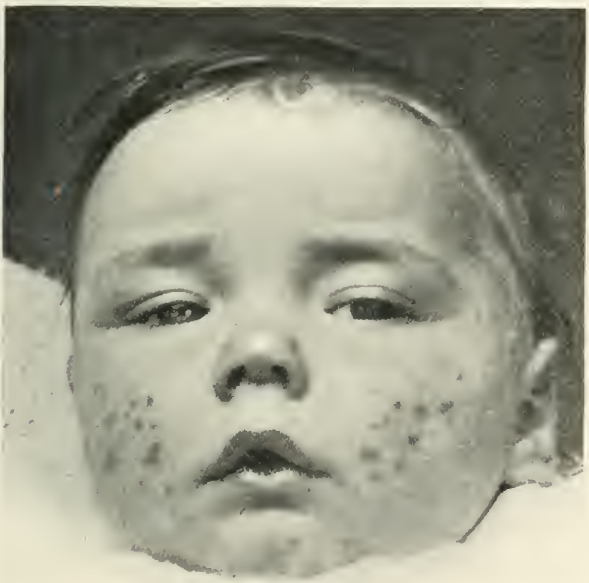
Post-mortem showed very little. Fatty change of a moderate extent was present in the heart and liver. Spleen 295 grm., soft but not diffluent. Kidneys 315 grm. ; capsule stripped easily, surface smooth, distinct honeycomb marking. On section proportion of cortex to medulla was normal. Cortical markings distinct and not distorted. Glomeruli more prominent than normal. Brain normal. Glands around right internal and external iliacs were much enlarged and soft. Those on left slightly enlarged. There was no evidence of tubercle in any part of the body.

ACNE IN AN INFANT.

WALLACE BEATTY, M.D., AND JOSEPH W. BIGGER, M.D.

Clinical Account by Wallace Beatty.

Christopher M—, aged 6 months, was brought by his mother to see me at the Adelaide Hospital, Dublin, in June, 1923, for an eruption on



Acne in an infant.

the cheeks which had started before the child was 3 months old. He had acne papules and pustulo-papules on both cheeks, with a few tiny comedones among them—a few comedones were present on the lower lip and chin. The skin of the nose and forehead was shiny. A smear I made from expressed sebaceous matter and stained by the Gram-Weigert method showed cocci, and bacilli which had the microscopic characters of the microbacillus of seborrhœa (acne bacillus). No oil or application had been used by the mother on the child's face previously.

Bacteriological Account by Joseph W. Bigger.

The small bead of sebum which I received from Dr. Beatty was inoculated into De Korté's medium* (broth containing 1 per cent. of glucose and 1 per cent. of oleic acid), and grown under anaërobic conditions at body temperature. After four or five days there was a profuse growth of a short, fat, Gram-positive bacillus, the microscopical appearance of which agreed perfectly with that of the acne bacillus. A *Staphylococcus albus* was also present but in smaller numbers than the bacillus. The occurrence of this bacillus in the lesions, its growth on De Korté's medium and its typical morphology satisfactorily establish its identity with the acne bacillus.

* *Lancet*, January 29th, 1923.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

Meeting held on March 15th, 1923, Dr. H. G. Adamson, President of the Section, in the Chair.

Dr. J. L. Bunch showed a case of *xantho-erythrodermia perstans*. The patient, a male, aged 47 years, first began to develop some small irregularly shaped flattish lesions on the chest one year ago. They were somewhat irritable and slightly scaly. During the past twelve months these first patches had increased in size and many more had made their appearance. The shape of many was somewhat oval with the long axis parallel to the direction of the ribs: others were more or less circular in outline and some were quite irregular in shape. The smallest patches were about the size of a sixpence, the largest about the size of the palm of the hand. They were distributed chiefly on the chest, some on the back and shoulders.

The itchiness and scaliness led him to suspect that it was a case of pre-mycosis, but the induration was hardly as great as would be expected in a case of this disease which had been present twelve months.

Dr. E. G. Graham Little showed a case of *folliculitis ulerythematosa reticulata*. Patient, a boy, aged 5 years. At present he had little more to show than the superficial pitting, characteristic of terminal stages of this disease, over the malar bones and forehead. The child was seen, when he was 19 months old, by Dr. MacKenna, who had kindly sent him the notes he then made. His diagnosis was: "An unusual variety of follicular hyperkeratosis with slight perifollicular erythema." Several of the follicular orifices showed spiny central projections but no suppuration. There were no subjective symptoms.

There had been very few cases of the disease. He thought he showed his first case there, and he did not know of another instance having been recorded. Eighteen months ago Dr. Darier had a case in Paris, and he sent him a description of it. McKee, in his original paper, reported three cases. As there were very few symptoms, probably a number of cases had been overlooked. All the cases had been in young children,

a slight majority of them in males. There was a history of tubercle in a small majority of the cases.

Dr. G. Pernet said he had recorded a similar case which he called atrophodermia reticulata symmetrica faciei. At that time he did not know that the condition had been previously described. The patient was a girl aged about 8 years.*

Dr. Knowsley Sibley said he had seen two cases of this condition at St. John's Hospital. One was in a girl, aged 18 years, who came to him two years ago with a very marked reticulate condition over her cheeks. At that time he could not properly name it, and he called it dermatitis reticulosa. He thought it was congenital, as the mother said the child had had red cheeks all her life. Sutton's book showed a photograph which was typical of his (Dr. Sibley's) case. She was given some eight one-third pastille doses of X-rays extending over about nine months. A few months later he sent for her to be photographed, but the condition had so much abated that the photographer said there was nothing left which would show in a photograph. The other case was in a young man, aged 18 years, who had the same condition of the cheeks, but not so marked as in the girl. His case was complicated by a good deal of acne in the lower part of the face, the remains of the old reticulated trouble being over the malar processes.

Dr. H. C. Samuel asked whether telangiectasis was a feature of these cases of McKee's disease. Some years ago he showed a case of what was generally agreed to be McKee's condition, and that woman had marked telangiectases. The diagnosis lay between lupus erythematosus and McKee's condition.

Dr. H. W. Barber said that Sir Cooper Perry had shown cases of the condition many years age, and he (Dr. Barber) did not think the disease was so rare as Dr. Little seemed to regard it.

Dr. Little replied that he did not think telangiectasis was a feature of the cases which had not been treated with X-rays.

Dr. E. G. Graham Little showed a case of *mycosis fungoides*. Patient, a male, aged 50 years. The condition for which he saw him a month ago was said to have begun with a mosquito-bite on the chest. It was probably a very typical case, but the diagnosis was so important that he wished to have the support of the Section. It was furiously, agonisingly itchy. There was much infiltration in the older patches, not so much in the newer ones. It had never receded, and had always extended, so that at the present time almost the whole trunk and limbs were occupied by large patches of infiltration. No tumours had yet made their appearance, but there was general glandular enlargement, especially in the groins.

Dr. R. Travers Smith showed a case of *abnormal scarring after chicken-pox*. Patient, a boy, aged 14 years, came to him to be examined three

* *Med. Press and Circ.*, May 31st, 1916, p. 487.

weeks ago. He had scars, some the size of a threepenny-piece, some larger, on the abdomen and back. When 16 months old he had had chickenpox; the lesions took a long time to heal, and the doctor was said to have put on them something which looked like paper: when this paper was taken away an ulceration was noticed, and that ulceration left scars. The boy had never been vaccinated.

Dr. J. H. Stowers said that possibly the scars, which were circular, of unequal size and distinctly cribriform in character, might be the result of vaccinia contracted in an unsuspected manner at the age of 16 months, when the patient was said to have developed the eruption from a recently vaccinated infant.

Dr. Whitfield suggested that this boy had had varicella gangrenosa infantum. It might be a secondary infection on varicella, or it might have nothing to do with varicella; possibly it was a form of ecthyma. In a number of cases the condition supervened on varicella, and when that occurred the ovoid form was lost; it became a large discoid lesion almost at once.

Dr. Dore agreed with Dr. Whitfield that the scars were probably due to gangrenous chickenpox.

Dr. Henry MacCormac showed two cases of *lupus vulgaris treated with potassium iodide*. Some time ago in a number of cases of lupus attending the Middlesex Hospital, the patients were given potassium iodide in large doses. This was done on a theory that the tubercle bacillus might be an acid-fast streptothrix—a view held by certain observers. The results were not uniform, and in the majority of cases little or no benefit took place. But in one of the earlier patients subjected to this treatment very marked improvement occurred. She was shown to-day as the first case. Investigations were made by Dr. Kingsbury into the complement-fixation of the series of cases, three antigens being used—*Actinomycosis bovis*, human tubercle bacillus, and an acid-fast streptothrix. It was found that in one case a partial fixation to the acid-fast streptothrix occurred, and this was the first patient shown to-day. The second case shown had also made considerable improvement under potassium iodide, and it was found that in her case there was also a partial positive complement-fixation to a streptothrix. The histories of the two cases are as follows:

Case 1.—Female, aged 27 years. Lupus developed on the face soon after birth, and on the buttocks at 14 years of age. She came under the exhibitor's care two years ago, and was put under large doses of iodides. She made marked improvement, but he found she had been previously under the care of the late Mr. Kellock, who had been using a similar

method of treatment. She had thus been for a considerable time under the influence of iodides. There was now very little evidence of active disease, the site of the former extensive lesions being replaced by a good scar.

Case 2.—Female, aged 16 years. The disease began six years ago, following suppurating glands in the neck, and spread over the face, involving the cheeks, nose, forehead and neck. There was also a patch over the left deltoid region which had apparently been cured by X-rays. This patient had been under treatment with iodides for some five months, and although there was still a good deal of disease present, a very marked improvement had taken place.

The patients in both cases had had some local treatment in addition to the iodides, but it may fairly be assumed that the improvement had in the main been due to the drug. The dose given had been 40 gr. of potassium iodide three times daily. This had been well tolerated.

These two cases were interesting because they both showed a positive complement-fixation to a streptothrix. Mr. Kellock used iodides in other forms of tuberculosis with benefit, and it would seem that in suitable cases, that was where either the form or the type of bacillus was different from that ordinarily met with as shown by the biological reaction, prolonged treatment with iodides might be attended with a considerable degree of success.

Dr. Knowsley Sibley said he had treated many cases of lupus with iodide of potassium, but he did not give the large doses of iodide which Dr. MacCormac mentioned; he gave it in the form known as nascent iodine. The patient took 20 gr. iodide of potassium dissolved in a tumberful of water after breakfast, then successive drinks of 1 oz. of chlorine water in home-made lemonade, four, six, eight and sometimes ten hours afterwards. He did not believe in large doses of iodide of potassium; the more iodide of potassium that was given, the less was it absorbed, and absorption was facilitated by giving small doses: 4-gr. doses he would regard as the maximum dose at one time. He had found this method excellent in the direct treatment of buccal mucous membranes: dusting diluted powdered iodide of potassium on to the ulcerated surface, then telling the patient to take some chlorine water into the mouth, and to hold it as long as possible, then to swallow it.

Dr. H. G. Adamson (President) said that iodine was a very old remedy for lupus vulgaris. It had been recommended by Liveing and, earlier, by the French physician, Lugol, after whom Lugol's solution was named. He (the President) had been giving Lugol's solution to lupus patients for several years past, and had given sometimes as much as 3 gr. of iodine three times daily. But in only a few cases had he seen any marked improvement, though in the "strumous" type of tuberculous skin affections and in tuberculous glands the improvement was often

striking. In lupus vulgaris he had never seen any improvement so pronounced as in Dr. MacCormac's cases.

Dr. Henry MacCormac showed a *case for diagnosis*. Patient, a male, aged 40 years, gardener by occupation. His duties included the care of a pony, which he stated suffered from some form of skin disease. The condition of which he complained began about fourteen months ago with a " scab " on the back in the region of the lumbar vertebræ. The lesion resisted all forms of treatment, and finally some form of operative procedure was carried out. In this region there was now a central crust covering a superficial ulcerated area about the size of a shilling, and surrounding it there was a scar some 3 in. in diameter. Beyond this again there was an area of pigmentation and telangiectasis. No X-rays had been used.

About one month after the appearance of the lesion on the back, the arms, head and legs were affected. On the arms and legs there were now well-marked areas, some small, some extensive, sharply circumscribed, with some atrophy in the more extensive lesions. At the periphery vesicles could be detected. In addition, on the legs there were a number of superficial erosions or ulcers presenting the appearance seen in a coccal infection. The Wassermann reaction was negative, and no ringworm fungus had been detected.

A small portion from the edge of one of the lesions was removed for microscopical examination. It presented the following features: collections of cells about the vessels of the corium and also well-marked superficial vesiculation.

Mr. J. E. R. McDonagh showed a case of *recurring erysipelas*. Patient had a primary sore on skin of penis in 1915. Treatment with three injections of salvarsan and six of mercury was instituted before the symptoms of the generalisation stage appeared. The treatment was not continued.

September 22nd, 1920: Patient appeared with a recurrent primary sore at the left peno-scrotal junction, and a generalised syphilitic eruption. The usual two years' treatment was prescribed and carried out.

October 10th, 1920: Patient had a rigor and fever and developed erysipelas of the penis and scrotum.

The second attack was in June, 1922, the third in September, 1922,

the fourth in December, 1922, and the fifth in 1923. The second and other attacks were not ushered in with fever. Each attack had left the penis and scrotum more elephantiasic than before.

This was not a case of syphilitic lymphangitis with fibrosis, but a case of recurring erysipelas due to the streptococcus of Fehleissen. The point of entrance of the streptococcus was on the site of the second sore. It could be recognised by a multiple vesicular lesion not unlike the commencing stage of herpes febrilis. The streptococcus had been found, and had recently been cultivated after considerable difficulty. So a vaccine was being prepared, as all other methods of treatment had proved unavailing.

Dr. H. G. Adamson thought that the condition called elephantiasis and leontiasis was generally of streptococcal origin, and due to repeated attacks of cellulitis (recurrent cellulitis), when it occurred in association with syphilis or with tubercle, and always when it occurred independently of these two diseases; but that elephantiasis associated with a syphilitic lesion was invariably of streptococcal origin was not in accord with the fact that in syphilitic cases the swelling sometimes subsided under anti-syphilitic treatment.

Mr. McDonagh replied that he had brought up the present case in order to show that many of the so-called cases of syphilitic lymphangitis were really of streptococcal origin. The differentiation was simple, because in streptococcal lymphangitis, although the streptococcus gained entrance through a destructive syphilitic lesion, the patient had many attacks, and each attack might be ushered in by fever and by a rigor. In true syphilitic lymphangitis the patient might either have no cutaneous lesion or else one which caused no break in the surface of the skin. Syphilitic lymphangitis was a progressive condition, and one which readily responded to treatment. Streptococcal lymphangitis was not influenced by antisyphilitic treatment, and not infrequently injections of arseno-benzene precipitated an attack of erysipelas.

Dr. E. G. Graham Little showed a case for *diagnosis; ? diphtheria of the skin.* Patient, a lady, aged about 65 years, who for some four years past had had almost persistent crops of pustules and vesicles covering the same parts always, *i. e.* both feet and the left hand, including all the fingers and the nail area. The whole affected foot area was of a darkish purple colour, very infiltrated, and the skin on the soles and dorsum of the foot was considerably thickened. On the mucous membrane of the palate she had a number of bright red vesicles, and she said she had had similar vesicular lesions on the tongue and sides of the buccal mucosa. Nothing had been found in the pustules except the common staphylococcus. Examination of an unbroken vesicle for tinea was negative of that diagnosis.

The only similar case he had seen was one he showed there four years ago, that of an officer, who, under the idea that his condition was syphilitic, had been two and a half years under treatment. His Wassermann reaction was persistently negative. He had an examination made of the surface in that case, and a diphtheritic organism was found—probably the true Klebs-Loeffler bacillus. He then confirmed this suggestion by saying that at least three diphtheritic attacks had followed in his wake; he had stayed at country houses, and diphtheria had broken out after his arrival. He improved greatly with diphtheria vaccine. Dr. Little thought the present case might be of the same nature.

Dr. J. M. H. MacLeod said he thought the affection might be ringworm, because of the scaly edge of the lesion on the foot, the condition of the nails of the hand, and the fact that only one hand was affected.

Dr. H. C. Semon agreed with the diagnosis of eczematoid ringworm. He said that recently he had had two or three such cases, but he had not been able to find the fungus. In eczematoid ringworm which became pustular, the fungus was rapidly destroyed.

Dr. E. G. Graham Little showed a case of *lichen planus atrophicus*. Patient, a female, aged 45 years. There were large areas of atrophic dermatitis, covering the nape of the neck, the armpits, the area underneath the popliteal space and the side of the legs. The lesions on the lower limb were definitely raised. So although there was atrophy, it was atrophy *en plateau*—the raised area—it was of an ivory-white colour. Formerly this plateau was red. Sclerodermia was an alternative diagnosis, but the history of the case and the distribution suggested to him the diagnosis he had offered.

Dr. W. J. O'Donovan showed a case of *muriatic acid erosion of fingers*. Patient, a man, aged 51 years. For twenty-two years he had worked as a galvaniser. His occupation consisted of dipping sheet-iron tanks into muriatic acid as a cleansing bath preparatory to a zinc galvanising process. His fingers were browned and blackened by acid. There were pits and fissures in the horny palms, and the finger-tips were swollen, sore and corroded into a filiform appearance. For two years although still at work he had been unable to cut up his own food owing to pain and tenderness of his hands; his wife had fed him. Other men at the factory were similarly affected.

Dr. W. J. O'Donovan showed a case of *carcinoma faciei apud puellam.* He was showing a second case* of multiple early squamous-celled carcinoma of the skin of the face of a young woman, aged 21 years. This case was of over nine years' duration ; it had a marked tendency to natural cure by scarring. The lesions, as in the previous case, were unilateral and below the ear, running like a livid band with a well-defined raised edge along the contour of the lower jaw. A microscope section of the case was also demonstrated.

Dr. A. M. H. Gray said that these cases were very interesting, and he did not know of any description of them elsewhere. They were different, clinically and pathologically, from the so-called Pagetoid basal-celled carcinomata. Having once seen a case, the condition was diagnosable clinically.

Dr. H. G. Adamson (President) agreed with Dr. Gray. These growths only resembled the Pagetoid condition in their consisting of large flat patches. Dr. O'Donovan was to be congratulated on having discovered a new type of epithelioma of the skin.

Dr. A. M. H. Gray showed a *male and female acarus extracted from one burrow.* This specimen was obtained from the fourth toe of the left foot of a man who had had scabies for four years. The burrow was about $\frac{1}{4}$ in. long, and with a lens two acari were visible in it. The first, at the end of the burrow, was a female ; that behind it, a male. The exhibitor had never before succeeded in finding a male acarus in the skin. It was generally thought that the male acarus wandered about the surface and did not burrow. J. W. Munro† had, however, shown that the male acarus only came in contact with the immature female before she started making her long burrow. The immature female and mature male burrowed very closely together, or even in the same short burrow ; the male impregnated the female, then the female left that burrow and started one on her own account, the male never coming near her again. When she had laid all her eggs she died. It was possible that in his case the male might have been in a tiny burrow adjacent.

Dr. M. G. Hannay showed a case of *cutis verticis gyrata.* The case will be published in full in a future number of this Journal.

Dr. H. W. Barber showed a *case for diagnosis.* Ever since this patient could remember she had had a skin which, when cut or scratched,

* For the first case, see *Brit. Journ. Derm. and Syph.*, 1923, xxxv, No. 2, p. 70.

† *Journ. Roy. Army Med. Corps*, 1919, xxxiii, p. 22.

separated, leaving, in the case of a cut, a gaping wound, and this took longer than normally to heal; and during the last few years she had large hæmorrhages under her skin. When first he saw her, the left arm from the elbow downwards was a large swollen bruise. She bled over her patellæ and elbows, and there were collections of blood there. Her skin felt loose like the skin of a puppy, and it could be picked up off the subjacent tissue. He thought there was a lack of subcutaneous tissue, and that the blood-vessels, being unprotected, were easily ruptured; but on excising some skin yesterday he found there was plenty of subcutaneous tissue. She did not bleed unduly when teeth were extracted. The question of dermatitis artefacta could be excluded.

Dr. Dore referred to a case of Sir Malcolm Morris, an elastic-skinned boy, who had congenital dislocations and who bled very easily; he had hæmorrhages of skin and joints, and small neurofibromatosis tumours. When he cut himself the edges separated and muscular tissue came into the wound. These tumours consisted of a fibrous capsule containing colloid material.

Dr. F. Parkes Weber thought there were two kinds of so-called "loose skin" or "chalastodermia." In one there was an excess, or relative excess, of elastic elements, and the ordinary white connective-tissue elements were diminished or defective in some way, and the skin was imperfectly attached by the subcutaneous tissue to the deeper structures; this was the true "elastic skin." In the other there was a degeneration or insufficiency of the elastic elements, and an increase in the ordinary white connective-tissue elements; so that, as a result of the connective-tissue hyperplasia and the diminution of true elasticity, the skin and subcutaneous tissue tended to become "baggy," or to fall in a pouch-like or flounce-like manner over the parts of the body below it.

Meeting held on April 19th, 1923, Dr. H. G. Adamson, President of the Section, in the Chair.

Dr. George Pernet showed a case of *disseminated lupus erythematosus associated with Raynaud symptoms and early sclerodactylia*. The patient was a single woman, aged 45 years. Ever since childhood she had had chilblains. At times some of the fingers went dead and then became bluish. Both little and ring fingers were permanently flexed, were more or less cyanosed, and to some extent atrophied, especially the terminal phalanges. Several of the fingers at their ends exhibited more or less circular shallow sulci (ainhum-like). The lupus erythematosus lesions were scattered about the fingers and backs of hands, and to a much less extent about the palms. Many of them were atrophied. On the outer sides of the extensors of the forearms were a number of similar lesions.

In the middle of the back there were a number of irregularly contoured islands consisting of atrophic areas with reddened periphery. There was one small elongated oval lesion of lupus erythematosus on the back of the tip of each shoulder (quite symmetrical). About and on the ears there were reddened areas, and a palm-sized characteristic area of lupus erythematosus on the anterior part of the vertex of the head. There did not appear to be any history of tuberculosis (phthisis, etc.) in the family, but twenty-five years ago tuberculous glands were removed from the patient's neck.

Dr. Wilfrid Fox showed a case of *parapsoriasis—type Xantho-erythrodermia perstans*. Patient, a male, aged 54 years, was under the late Dr. Crocker in 1903, who diagnosed his condition as stated in the above title. Dr. Crocker was anxious to show him before the old Dermatological Society of London as a typical case, but the patient was unable to come. The condition had never cleared up during twenty years: the patient had been sometimes better and at others worse. When the exhibitor first saw him on February 21st there were numerous oval patches, reddish brown in colour, lying obliquely on the trunk in the axis of the ribs, similar to the arrangement often seen in pityriasis rosea. On the arms the lesions were eczematoid and in places lichenified. The treatment he has received has been tab. parathyroid $\frac{1}{240}$ gr. and β-naphthol ointment, 2 per cent.

Dr. Haldin Davis showed a case of *pityriasis lichenoides chronica*. This was the third time that this boy (now aged 12 years) has been shown to the Section. He had suffered from the eruption, which had maintained almost the same state, since he was 3 months old. Dr. Graham Little showed him when he was very young, and he (Dr. Davis) showed him three years ago. His diagnosis (which was also that of Dr. Little) was pityriasis lichenoides chronica, a variety of parapsoriasis, in which the lesions were very minute. The chief reason why he was showing the patient to-day was that about three months ago Dr. MacCormac exhibited a case with lesions that seemed to him exactly similar to those visible in this case, but which he thought would clear up; and he was anxious for Dr. MacCormac's opinion on this case. It would be noted by members that the lesions in this patient were minute, scaly papules, scattered over

the trunk and limbs, but absent from the face, hands and feet. Many ointments had been tried, but as yet the lesions had been resistant to every treatment employed.

Dr. J. H. Sequeira showed a case of *congenital onychogryphosis*. He brought the child, aged 2 years, in order to ask assistance as to treatment of the nails. The child was born at the seventh month, and the nails were not developed at birth. When they did develop they grew in an hypertrophic form, which resembled onychogryphosis. All the nails of both hands and feet were affected. The hypertrophied nails were strong, brownish in colour, and projecting upward from the nail-beds for from $\frac{1}{4}$ to $\frac{1}{3}$ inch. There were two other children in the family, and they were normal and healthy, and there was no history of a similar condition occurring in the child's relatives or forbears.

Dr. Graham Little said he had had an exactly similar case; he showed it at the meeting of the Dermatological Association in London eighteen months ago. That child was a little younger than Dr. Sequeira's patient, and the nail condition was not noticed at birth. Atrophic nails developed on all the digits in the same way; previously there had been chronic impetigo. He did not succeed in getting any help in regard to treatment of that case. The nails were cut with clippers from time to time in order to remove the local discomfort.

The President recommended evulsion of the nails followed by scraping of the roots and nail-beds. He thought it would be necessary to destroy the nail growth entirely; the child would be less uncomfortable with no nails than with nails such as these.

Dr. L. A. Savatard showed a case of *xanthoma (? diabeticorum)*. Patient, a married woman, aged 33 years, first consulted him on April 10th this year. She presented numerous typical xanthomatous tumours of the skin, varying in size from that of a pin's head to that of a large pea. The tumours were yellow in colour, and were for the most part discrete. They were situated over the posterior aspect of both elbow-joints, in the left anterior axillary region and on the buttocks. There was also some slight infiltration of the flexures of both palms. The patient also complained of pain in the right heel at the site of attachment of the tendo Achillis, and suffered, too, from pruritus vulvæ. Occasionally shooting pains ("like red-hot needles") were experienced in the lesions, which were always painful on pressure. The tumours were first noticed three years ago in the neighbourhood of the right shoulder, and then shortly afterwards appeared in the other areas. Some lesions had been removed

by the actual cautery, and had not recurred; none had involuted spontaneously. The urine had been repeatedly examined, and had always been free from sugar. At the last examination (April 13th) it was acid, specific gravity 1018, and contained no albumin and no sugar. Her sugar-tolerance curve was practically normal. Dr. A. Howarth (Pathological Department, Manchester University) conducted this test and reported: "I have seen this type of curve in an apparently normal person at a time when he was not feeling up to the mark. . . . This is certainly not a diabetic curve." He had thought that perhaps the curve would show that the patient was a *potential* diabetic, but it did not suggest even that.

As a child the patient suffered from recurrent attacks of "gastric ulcer." In 1914 (at the age of 24 and two years after marriage) she was operated upon for a perforated appendix, and at the same time a hysterectomy was performed and her appendages were removed. In 1921 the patient saw a consulting surgeon, who diagnosed a twisted kidney. The family history was bad: her mother died, aged 48 years, from diabetes; her father, aged 67 years, from heart disease; two brothers, aged 39 and 29 years, from phthisis; a sister died from abdominal tuberculosis; and another sister, aged 47 years, from phthisis. There were two sisters alive and well.

Although therefore this case presented no evidence of diabetes, he anticipated, in view of her family history and of the records of other similar cases, that diabetes would supervene later, and therefore suggested that this should be classed as a case of xanthoma diabeticorum.

Dr. F. Parkes Weber said he did not think that in cases of nodular xanthoma of this kind anyone was justified in saying that probably diabetes mellitus would supervene, especially if ordinary care in diet were taken; there were not sufficient known facts to justify such a view. But he quite agreed that the xanthoma in Dr. Savatard's patient belonged to the same class as that which occurred in glycosuric and diabetic patients.

Dr. A. Whitfield said it was probable that in future xanthoma diabeticorum and xanthoma tuberosum would be merged into one classification. It was, apparently, clear that most cases of xanthoma tuberosum had cholesterolæmia, and in cases of diabetes which developed xanthoma diabeticorum there was also cholesterolæmia; and it was probably associated with that side of the function of the pancreas rather than with the sugar part of that organ. In the case of Harrison and himself, Harrison found evidence that the proteolytic side of the pancreas was working badly; and the speaker thought it was so in the present case too.

Dr. Graham Little said he had seen a very interesting clinical case, almost exactly like this, of a surgeon who had similar xanthoma lesions on elbows and buttocks. They were treated with X-rays, and for a time they improved. When he was seen there was no glycosuria at all, but eventually he died with acute diabetic coma.

Dr. A. M. H. Gray expressed his agreement with Dr. Parkes Weber and Dr. Whitfield. And he did not think there was evidence yet that the cases of cholesterolæmia seen were necessarily associated with hyper-glycæmia, or with pancreatic disease. He supposed there was no doubt the lesions were due, not to hyper-glycæmia, but to cholesterolæmia.

Dr. Savatard also exhibited photographs and sections of a case of *multiple epidermoid cysts.*

Dr. H. W. Barber showed a case of *adult urticaria pigmentosa.* Patient, a male, aged 25 years, first noticed the eruption on his chest in 1918. Six months ago it spread to the back and arms, after an attack of severe indigestion, probably caused by eating tinned food while on a river holiday. He now had a profuse eruption of urticaria pigmentosa all over him, and the wheals were visible at places where he had scratched and rubbed. There had recently been published a case, with discussion, shown by Dr. Simon in Paris, in which the eruption appeared for the first time when the patient was 52 years of age. Two interesting facts were brought out in connection with it. One was, that the eruption appeared after the patient had had severe indigestion, with fever, and it was probably typhoid fever, because later he developed a typhoid abscess in bone. The other point was that he was syphilitic.

He thought it was questionable whether adult cases were of the same nature as those in children. He thought the ordinary infantile urticaria pigmentosa was a nævoid condition, and he believed Darier shared that view. He thought the adult form must be a toxic eruption, and if one were to collect cases and investigate them systematically, the cause might be discovered.

Dr. MacLeod said that, in the absence of a definite finding of mast-cells in the tissue, it did not seem to him that a diagnosis of urticaria pigmentosa was warranted.

Postscript.—Histological examination of an excised lesion showed the presence of a large number of mast-cells.

Dr. H. C. Semon showed a case of *unusual localisation of ichthyosis.* This child, aged 5 years, was born with ichthyosis of the lateral aspects of

the neck, flanks, and slightly on the back. The condition had persisted and led occasionally to friction and drying effects in these areas. There was no familial history of a similar condition in the parents or their near relatives. The interest of the case lay in the very unusual localisation.

This case seemed to belong to that variety of bilateral symmetrical type which found a rare but highly characteristic expression in keratosis palmaris et plantaris hereditaria, or tylosis. Cases of this kind seemed to supply rather strong evidence against the theory of thyroidal causation or influence in production. A cretin with ichthyosis had yet to be recorded.

Dr. F. Parkes Weber thought Dr. Semon was right in suggesting that hyperkeratosis palmaris et plantaris might be allied to various kinds of congenital hyperkeratosis elsewhere. He thought there was a large group of congenital or developmental hyperkeratoses, including various forms of congenital ichthyosis and various forms of hyperkeratosis affecting the hands and feet. Sometimes the hyperkeratosis was of punctate distribution. He thought that in rare cases the local superficial blood-vessels were likewise involved in the congenital abnormality of growth, and that the cases described as congenital erythro-keratosis of the palms, etc., belonged to the same class. All these were varieties of nævus-formation, and the congenital hyperkeratosis of acroteric distribution, of the "tylosis" kind, was one of the most remarkable. He thought that the case which had been shown by Dr. Haldin Davis might really be one of punctate hyperkeratosis of generalised distribution, and therefore might really belong to the same class as Dr. Semon's case.

Dr. H. C. Semon showed a case of *gas-burn scarring*. This man was very extensively burned by direct contact with the fluid of mustard gas at Arras in 1918. The convex surfaces of the back and buttocks from neck to thighs were involved, whilst the loins and interscapular areas appeared to have entirely escaped. The scarring was regular and quite superficial, and there was no tendency to contraction, as after acid or burns by scalding or dry heat. Except for one small nodule on the apex of the right shoulder there was no keloid formation. The scarred areas were white in colour, but pigment was excessive for several inches beyond the affected parts. The follicles appeared enlarged and patulous, owing, as had been suggested by Dr. Adamson, to destruction of the normal, superficial openings.

Dr. O'Donovan said he had seen a man who was extensively burned in the manufacture of nitric acid, and he at first thought the case now shown was another of the same kind. The nitric acid lesion had a small keloid.

Dr. H. W. Barber said he had five mustard-gas burns on his arm and the

skin was smooth. But the worst burn resembled an X-ray burn, and that took two and a half months to heal, and pigmentation remained. The point of interest about mustard gas was that, like chrysarobin, it was soluble in fats and not soluble in water. He found that the vapour always picked out the sebaceous areas, probably because it was fat-soluble.

Dr. S. E. Dore mentioned a case of *breast tumour with atrophy of skin which had been shown at a previous meeting*. The following report had been received from Dr. Dudgeon :

Report on Dr. Dore's Case of Tumour of Breast, by Dr. Leonard S. Dudgeon.

"Sections of the skin show an irregular surface which corresponds with the appearances noted on clinical examination when the skin was lying loose. There is no increase of pigmentation. A mononuclear reaction is present in the fibrous tissue adjacent to the epidermis. Between the surface layers of the corium and the deep tissue, which is highly cellular, the fibrous tissue shows a well-marked hyaline change. Sweat-glands and sebaceous glands are present ; also numerous islets of unstriped muscle and nerve-fibres. In the deepest layers large hæmorrhages are present, and also well-defined hæmangiomata, which could be recognised on clinical examination, and were very obvious in the deepest tissue in the portion removed for microscopy. The deepest layer of fibrous tissue is intermixed with the normal fatty tissue which it has partially replaced."

Note by Dr. Dore.—The general opinion, expressed by several of the members who had seen the sections, was that it was a neurofibroma.

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY.

The Third Annual Meeting was held at Liverpool on Tuesday and Wednesday, July 10th and 11th, under the Presidency of Dr. Leslie Roberts. On Tuesday morning, after the Annual Business Meeting had been held, a discussion took place on "The Physiological and Pathological Conditions Governing the Pattern and Distribution of Cutaneous Reactions." Dr. H. G. Adamson opened with a very complete general survey of the subject, and he was seconded by Dr. S. E. Dore, who dealt especially with modern work on the

physiology of the capillary vessels. The subject was thereafter discussed by Drs. MacLeod, Goodwin Tomkinson, Barendt, J. H. Sequeira, Rupert Hallam, Savatard, Prosser-White, E. F. Skinner and the President.

Dr. Whitfield read a paper on a case of "Fox-Fordyce Disease," the examination of which had enabled him to bring forward a new view as to its ætiology. The paper was discussed by Drs. Gibson and Barber.

Dr. Graham Little then described, under the title of "Erythematoid Benign Epithelioma," a series of cases of multiple, flat, rodent ulcer, some of which had been previously shown by him at the Royal Society of Medicine. The paper was discussed by Drs. Barber, Gray, Savatard, Tomkinson and Whitfield.

On Wednesday, the morning session opened with an exhaustive paper by Dr. Wilfrid Fox on the question, "To What Extent can the Wassermann Reaction be Depended Upon for the Diagnosis and Treatment of Syphilis?" It was much to be regretted that Dr. Wilson, who should have followed, was prevented by illness from being present. The discussion was continued, however, by Drs. Whitfield, Gray, Mallam, de Jong, Barendt, Skinner, Graham Little and David Lees.

Following this, Dr. Savatard read a paper on a case of "Bowen's Pre-cancerous Dermatosis," and this was discussed by Drs. Barber, Shelmire (U.S.A.), Adamson, Whitfield, Graham Little and Gray.

In the afternoon of both days of the meeting cases of unusual dermatological interest were exhibited.

On Tuesday members of the Association were entertained at dinner by their Liverpool colleagues at the University Club, which institution had kindly thrown open its house to members during the meeting.

The meeting was a most successful one, both from the point of view of numbers attending and from the work done, and the Association is greatly indebted to the Council of the Liverpool Medical Institution and to the Committee of the University Club for placing their buildings at the disposal of the Association, and also to Dr. Leslie Roberts and his colleagues in Liverpool for their hospitality, and for the trouble they took in collecting cases for exhibition.

It was agreed to hold the next meeting, in 1924, in London, and Dr. H. G. Adamson was elected President for that year.

CURRENT LITERATURE.

INFLAMMATIONS, ETC.

FUR DERMATITIS. A. C. Roxburgh. (*Brit. Med. Journ.*, 1923, p. 534.)

In a letter, Roxburgh points out that but a small percentage of the total wearers of "beaver coney" collars suffer from dermatitis, also the length of time for which the furs are worn before the appearance of the rash varies from two to twenty weeks. He suggests that these facts may be explained by a very gradual development of sensitiveness to the irritant. In support of this he mentions a patient who took eleven weeks to develop the rash on her neck, and who, at his suggestion, then carried the collar over her arm for a few minutes. Within twenty-four hours she developed typical lesions on her wrist.

Walter F. Castle. (*Brit. Med Journ.*, 1923, p. 535.)

A list of the chief dyes used is given in a letter:

Light brown	Pyrogallic acid.
Medium brown . . .	Metatoluylene diamine base.
Dark brown	Metaphenylene diamine base.
Red brown	Para-amido-phenol-chlorhydrate.
Deep black	Paraphenylene diamine.
Blue black	Nigrosine and nigrosine with paraphenylene diamine.

In the preparation of the furs the hair is first cleansed of grease by means of soda, soap lye with ammonia or milk of lime. To increase the affinity of the hair it may be soaked in bleaching powder solution and hydrochloric acid. For dyeing, one of the amines, commercially known as "ursol," "furol," "fantols," etc., is used. When darker shades are required the skins are first mordanted with potassium bichromate or the sulphates of iron and copper. The mordants are not neutralised in the cheap furs, and he therefore suggests that some suspicion attaches to the strong chemicals thus used as well as to the dyes themselves.

Henry C. Semon. (*Brit. Med. Journ.*, 1923, p. 613.)

The correspondence column contains an analysis of the dye by Skinner, quoted by Semon. The tests point to the metaphenylenediamine base, which is actually more poisonous to the skin than is the "para" isomer, and to a bichromate mordant. The dye is soluble in saline and in wool-fat. Semon points out that these have their analogues in the sweat and sebaceous secretions. M. S. T.

HEREDITARY TYLOSIS. J. D. Rolleston. (*Brit. Journ. Child. Dis.*, January–March, 1923, xx, p. 16.)

A typical case is reported in a girl, aged 2 years, in whose family the condition could be traced through five generations. A brief *résumé* of the literature is added. W. J. O.

RADIOLOGICAL AND CLINICAL STATES OF THE ALIMENTARY TRACT IN ECZEMA. Urbach. (*Arch. f. Derm. u. Syph.*, January, 1923, cxlii, 1, p. 29.)

Internal causes of the pathology of cutaneous diseases hold the field in all contemporaneous literature, and the investigations here recorded are illuminating and progressive.

According to Ehrmann, the mechanism of eczema may be visualised and explained by the hypothetical absorption in the gastro-intestinal tract of relatively large protein molecules as a result of defective catabolism. These toxins are carried by the circulation to the papillary body, where by their irritation they may lead to simple exudation ("spongiosis") or to stimulation of the neurovascular mechanism ("urticaria factitia"), or the nerves of sensation ("pruritus")—common associates of every case of eczema. Local toxæmia results in sensitisation, and a slight external stimulus is then all that is needed to produce a typical eruption of eczema.

The conception is fascinating, but the ultimate explanation is probably more complex, and no investigator has as yet succeeded in isolating the chemical bodies responsible.

To thirty-two eczematous patients of all ages and both sexes Urbach gave a test meal of 30 grm. of white bread and 300 grm. of weak, unsweetened tea. The stomach contents were examined before and after the test-meal in each case.

Total acidity before test-meal.		Total acidity after test-meal.	
No free HCl . . .	8 cases.	No free HCl . . .	10 cases.
Slight	1 case.	Free HCl 2–10 . . .	13 „
Free HCl 11–20 . . .	3 cases.	„ „ 11–20 . . .	5 „
„ „ 40 . . .	2 „	„ „ 21–28 . . .	4 „

In 18 cases no contents obtained.

These results agree in the main with those published by Ehrmann. (The majority of 150 cases examined in the last eighteen months also exhibited hypo-acidity. It is well known that among other functions the gastric HCl initiates digestion of connective tissue and vegetable matter, disinfection in the upper part of the small intestine, and specific stimulation of the secretion of trypsin.

It therefore follows that most cases of hypoacidity also manifest symptoms of intestinal inefficiency, which lead often to constipation or diarrhœa. The pepsin-HCl content of the stomach would appear to depend on four factors: (1) the volume of NaCl and other chlorides in the circulating blood; (2) the condition of the gastric glands; (3) the influence of the nervous system; (4) the constitution of the individual.

Arnoldi states that in the hypo or anacid gastric states, the chlorine and hydrogen ions in the blood are always reduced, while it is a well proven fact that the vago-sympathetic connections of the stomach and intestines are intimately associated both with their motility and secretory functions.

Radiological observations, of which these are claimed to be the first on record in such cases, revealed the following:

Stomach.

Hypersecretion— (which it is admitted may include regurgitation from duodenum, swallowed saliva, defective absorption of fluid in the meal, or passive transudation of fluid from the gastric vessels.)	13 cases.
Hyperperistalsis	5 „
Hypermotility	7 „
Gastroptosis with elongation	8 „
Atony	5 „
Hypotonia	3 „
Bottle-stomach	1 case.

Intestines.

Enlarged sigmoid and prolapsed transverse colon were found to coincide with clinical manifestations of severe constipation, and in these cases putrefactive tendencies were doubtless the inevitable results of stasis.

It is interesting, also, as showing the wide sphere of influence in alimentary dyscrasia, that in six blood examinations made five cases showed marked lymphocytosis and four eosinophilia. For reliable data the above records would seem to entail both the biochemical and radiological examination of every case of eczema (*e. g.* hypersecretion, as evidenced by excessive fluid contents of the stomach on the fluoroscope, will need control by the laboratory examination of the gastric contents, etc.).

The principles of treatment as based on these findings are supplemental to the immediate alteration of local manifestations by lotions, ointments, etc., and if indicated, surgical intervention as a first measure (*e. g.* appendicectomy, colopexy, gastro-enterostomy, etc.).

The differential diagnosis of functional and organic disease of the stomach is important, and search should also be made for such primary causes as dental caries, antral disease, tuberculosis and the like. Briefly, the investigation must include a very thorough general examination on modern lines, with such control of the diet as is indicated by the gastric findings.

In cases of hypoacidity with some free HCl present, acid. hyd. dil. ♏x *t.d.s.* ¼ hour before meals are indicated; where there is complete achylia, long-continued administration of pepsin and hydrochloric acid has a very beneficial effect, and in so-called constitutional cases it is better to treat the individual rather than his stomach.

Sodium bicarbonate is very useful in those cases in which there is pronounced intolerance to acids of any kind.

Hypersecretion demands a diet which counteracts it, and reduces motility of the musculature. Milk, cream and butter should be given in excess, and most medicaments are contra-indicated. H. C. S.

THE NATURE OF ECZEMA. H. Jaeger. (*Ann. de Derm. et de Syph.*, January and February, 1923, pp. 10–34 and 109–129.)

The writer conducted a large number of experiments to ascertain whether eczematous and certain other diseased skins are differently or more readily affected by external agents than the skin of normal persons. The chemicals chiefly tested were: formalin 4 per cent., oil of turpentine, and tincture of arnica. Lint saturated with one or other of these solutions, under an impervious dressing, was fixed to the healthy skin of 140 persons for twenty-four hours. When removed the results were noted. In like manner 77 patients suffering from eczemas of different types were selected and the sound parts of their skin subjected to an identical routine. The following facts were elicited. Only 4 per cent. of the skins of normal people showed any reaction to these chemicals. On the other hand, of the eczematous sufferers, 51 per cent. developed, on the sound part of their skins, a marked eruption. Macroscopically and microscopically the lesions were indistinguishable from an acute vesicular eczema. A few did not advance beyond the erythema stage. Ten per cent. of the healthy areas on the skins of a few invalids affected with a variety of lichen, submitted

to the same experiments, broke out with an eczematous rash. Of the seborrhœic cases similarly tested only 8 per cent. acted positively.

This marked irritability of the eczematous skin to chemical agents Jaeger regards as an hereditary or acquired individual character. He thinks it probably arises from the same weakness or tendency which causes idiopathic eczema. He concludes that its seat is more likely to be situated in the cells of the skin—a tissue idiosyncrasy—rather than in a humeral defect or excess, present in the blood-lymph.

This paper may be helpful from the sidelight it may throw upon the incidence of the occupational dermatoses. R. P. W.

SOME POINTS IN THE ÆTIOLOGY OF ECZEMA. J. Ferguson Smith. (*Glas. Med. Journ.*, March, 1923, p. 160.)

All the latest and attractive theories are discussed, including that which assumes a catarrhal condition of the bowel to be present and to permit of the passage of unsplit proteins into the general circulation. The author believes that sensitiveness to protein is specific and not general, and that seborrhœic patients are more liable than others, thus explaining the hereditary factor. Smith made cultures from the eczematous areas in fourteen patients, and in one case the organism, killed and applied in a weak alkaline solution to a non-eczematous portion of the patient's skin, caused definite signs of inflammation. He regards this experiment as very suggestive. W. F. C.

SKIN ERUPTIONS FROM GASTRO-INTESTINAL DISTURBANCES. A. Ravogli. (*Urol. and Cut. Review*, March, 1923.)

The only point of interest in this article is the report of a case of toxic erythema following ingestion of creasoti (two doses of ten drops) and subsequent gastro-intestinal disturbance. W. H. B.

QUARTERLY SURVEY OF DERMATOLOGICAL LITERATURE.

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DERMATOLOGY AND SYPHILIS

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SYPHILIS IN THE FIFTEENTH AND SIXTEENTH CENTURIES, ESPECIALLY AT PARIS.*

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In the year 1496, Sister Jehanne Lasseline, a sister and prioress of the Hotel Dieu of Paris, inscribed to her account ending the last of September the disbursement of eighty pounds paresis for patients having "the great pox of Naples." This financial item of Sister Jehanne is the oldest known document indicating the existence of syphilis in Paris.

It is, nevertheless, averred that the disease had flourished for already two years in the capital when the Hôtel Dieu first mentioned it in its books, because the famous decree pronounced by Parliament during the last days of the year 1496 declared that "the contagious disease called the great pox" had been "rampant for two years, both in this city of Paris and in other places."

Did syphilis come from Italy with the armies of Charles VIII? Was it imported by the Jews expelled from Spain by the Inquisition?(1) Had it not been smouldering unrecognised in the Parisian lazar-houses for years? All evidence of the epoch only permits of very slim conjectures in this respect.

But what can be formally asserted is that at the end of the fifteenth century a cruel epidemic, of unknown nature up to that time, visited the greater part of Europe, in France called *le mal de Naples*, in Italy *le mal Français*, here and there "the great pox" (*la grosse vérole*), and that it was already rampant in Paris in 1495.

* A lecture delivered to the Medical Society of Geneva, June 1st, 1922.

Syphilis of the present time—occasionally very severe in its manifestations—is only a shadow of what the contemporaries of Charles VIII suffered from it. From the very onset the disease was truly very fearful. Those contracting it soon became the object of terror and disgust. The ulcers covering the body and corroding the tissues to the bone, gave forth such a stink that, according to popular belief, it was quite enough to smell it in order to become infected.

Hence nobody would speak to them, nay, even lay eyes upon them, much less to dwell near them. Forcibly ejected from every quarter they roamed aimlessly about, living from hand to mouth as best they could. They were seen to die in the streets of Paris and in the fields beyond the city.

At Paris the number of victims soon attained such a high figure that Parliament found it necessary to act. Now, under Charles VIII, the public powers were little familiar with half measures. The decree of March 6th, trumpeted in all the public squares, is quite sufficient evidence in respect of this.

It was decreed that every syphilitic within the precincts of Paris could not leave his house until completely cured of his disease, allowing only visits from the priest and the churchwardens of their parish, who brought them food. The homeless poor were consigned to the borough of St. Germain, without the walls of Paris, and infected foreigners were ordered to quit the city within twenty-four hours. The gibbet was awaiting all refractory persons.

It must have been uncanny to look upon this procession of syphilitics fleeing in masses from the inhospitable city, which had no better remedy than the rope to offer them. At the two extremities of Paris, in front of the barriers of St. Denis and St. Jacques, guardsmen were stationed to take the names of the exiles, and gave to each, as succour for their journey, the sum of four sous paresis. The Prevost's servants, who closed the portals of the city and placed chains across the Seine, were instructed to look out for and prevent " any patient with the disease to enter openly or secretly into the city of Paris."

The place chosen for receiving vagabonds ill with syphilis was a dependence of the celebrated Abbey of St. Germain, whose three romanesque towers dominated over the fields at the south-west of the city, and it was not far from here that the syphilitics were housed.

Parliament bought two large barns, which, according to the cartularies

of the chapter of the Abbey, formed the angle of the Chemin de Sèvres and the Rue du Sépulcre. Quests, taxes and the products of certain fines covered the expenses of a summary installation which soon could lodge and feed indifferently the contaminated needy. Thus the first hospital in Paris for venereal disease was founded.

Isolated, hunted down or hung, there was apparently nothing more to be feared from syphilitic persons—at least so the Parisians must have thought. In reality, how could they have supposed that the terrible decree was at the same time useless and impracticable, that a single case overlooked was enough to revive the insufficiently extinguished conflagration, that a number of apparently healthy inhabitants were already infected and spread the fatal germ, and finally, that persons released after a few weeks of detention were all the more redoubtable for the public health the greater their appearance of recovery?

Consequently surprise was great when syphilis re-appeared in the capital. The year was not completed before the diseased again filled the streets. They were again to be seen, braving the measures promulgated against them, going about in broad daylight and even begging in front of the Palais des Tournelles, under the eyes of the King.

In the spring of 1498 the danger became still more threatening, because the unexpected death of the young King and the accession of the Duke of Orleans to the throne attracted peasants, bourgeois and the nobility to Paris from every nook and corner of France to witness the obsequies of King Charles and the solemn entrance of Louis XII.

In the hope of protecting the people and the seigniory "confided to his vigilance," the Prevost thought it well to again resort to the decree of Parliament and its excessive severity. However, it should be said, a concession was made; in the future there would be no gibbet for the unruly poxed patient, because he would simply "be thrown into the river."

But all these measures were of no avail. In an agglomeration so considerable the epidemic found an easy prey within its clutches. Moreover, again this time, the clumsy expelling of the "infected" foreign element was the most disastrous consequence for the provinces which, up to this time, had not been contaminated with syphilis.

And it was not only poor France that was in the grip of this "new plague," which, if one is to believe Jacques de Béthencourt, was itself soon to become more frequent than all other diseases taken together.

Spain and Italy were the first to be ravaged, while Germany was not

long in becoming invaded. The mercenary troops which served in turn the king of France and the emperor sowed on their track the seeds of contagion, which the depraved Germanic customs caused rapidly to fructify.

In Scotland James IV menaced the syphilities of Edinburgh with the mark of a red iron on the cheek should they refuse to leave the city. At Venice the galleys of the fleet could not raise anchor because the entire crew of each was ill with syphilis. Every day showed a progress in the geographical progression of the scourge, which in less than two years had contaminated more than the twentieth part of the population of Europe. Hence the last hour of the year was sounded in the midst of general consternation.

In fleeing—as did Galen on another similar occasion—from the epidemic, the Faculty of Medicine of Paris left the field open to the zeal of the surgeons. The brotherhood of St. Cosmos were careful not to allow such a splendid opportunity to escape it, and immediately set about to treat le mal de Naples, in the first place with cautery, arsenic and sulphuric acid, afterwards with mercury, which the Islamic and Chinese physicians had prescribed for centuries in cutaneous affections.

The panic having subsided the physicians again appeared upon the scene, and apparently approved the use of quicksilver, for the very good reason that they continued to prescribe it. But a cloud of empirics, charlatans and mountebanks had burst over the city during the storm, offering a most brazen competition with the medical profession in general. As can readily be surmised, the public rapidly became infatuated with all these healers, who, if they did not give back health, at least vended hope.

Now, in these unskilled hands, the best remedies became transformed into poison, this being especially true of mercury administered to anybody without rule or measure, with the result that its effects became disastrous. The people, prompt to confuse abuse with use, concluded that the medicament was responsible for the accidents, without comprehending that the ills were due to these illiterate impostors in whom it so readily confided. Physicians, for the most part, endeavoured to react against this general prejudice, but the malicious merely used it to their profit.

Then surgeons and barbers made fortunes by the sale of ointments guaranteed not to contain mercury, but being unscrupulous they were

ready at any time to resort to the metal, adopting as principle that the best remedy was the one that sold the best.

The National Library at Paris possesses a document on this subject, dating back to the early years of the sixteenth century. It is the advertisement of a master barber-surgeon who, with God's aid, without inunctions or sweating could cure syphilis with his elixir, likewise all the complications resulting from the disease. I give the text *in extenso*, as it has a peculiar savour of its own that would be lost by translation :

> " Plaise vous sçavoir qu'il y a aux faulxbourz Sainct Germain des prez ung maistre barbier et sirurgien qui est bien expert et bien experimenté et qui a faict plusieurs belles cures et beaux experimens en la ville de Paris et ailleurs, qui avec l'aide de Dieu garist de toutes malladies procedents de la grosse verolle curable, sans grever nature ne faire violence aux patiens. Et aussy garist le dit maistre de plusieurs aultres malladies segrettes et aultres qui ne sont pas isy declarez. Et le dit maistre garist par bruvaiges, sans frotter d'oingemente et sans suer. Et sy le dit maistre garist bièn aussy qui vouldra estre traicté pour faire la diete, le dit maistre le fera faire honnestement. Et premièrement garist le dit maistre de gouttes nouées ou à nouer, de nerfs retraictez et de vieilles ulceres, dartres à la main ou en aultre lieu, chancre en la gorge ou en la bouche ou au palais, avecques les cartillages alterez. Ou s'il y a quelque personnaige qui ait trou au palais et que à raison du dit trou le personnaige parle du nez, vienne par devers le dit maistre, et avec l'aide de Dieu il pourra bien parler. Le dit maistre demeure aux faulxbourez Sainct Germain des Prez . . . vis à vis (?) d'un patissier . . ."

I fancy that even in our time no charalatan has composed an advertisement that can surpass this venerable prospectus.

Whatever may have been the extent of public distrust, mercurial treatment nevertheless remained the one *par excellence*. Jacques de Béthencourt, the author of the first book on syphilis published at Paris, has left us interesting details in respect of mercurial treatment as carried out at the commencement of the sixteenth century.

When the weather became warm and soft, the patient, having been let blood and properly purged, was placed in a carefully closed and continually heated room. Here, twice a day, at the aurora and evening, he was submitted to inunctions before the fire, on the arms and thighs. The process finished, the patient was put to bed under thick bed-clothes,

surrounded by large sacks of hot barley in order to provoke diaphoresis, the object being to expel as quickly as possible all the peccant humour.

This being the object to attain, it was absolutely necessary to accomplish this by carrying out a severe diet. Beef and pork, fish, poultry and even eggs were considered detrimental. Therefore the menu was, of necessity, very limited. It only included some white meats, dried roots and barley —especially barley that Hippocrates and Galen declared to be detergent, emollient and tonic. Erosions of the tongue, lips and cheeks, loosening of the teeth, intense ptyalism and fœtidity, the too frequent consequences of the procedure, did not prevent the treatment from lasting a week, if not longer, and it was frequent to see patients undergo it upon three or four occasions.

In Germany things were far different. The patient, kept in a hot oven for nearly a month, carried out each day from two to four inunctions on the head, limbs, spine and umbilical region. The Chevalier Ulric von Hutten affirms—and one may readily believe him—that this barbarous practice resulted in the survival of hardly one unfortunate patient in one hundred.

The mercurial ointments, like the majority of remedies in vogue at this epoch, were prodigiously complex mixtures. One was in the age of gold and polypharmacy, and our present impoverished imagination can hardly conceive the frenzied *débauche* of formulæ to which the fantasy of the apothecary gave itself up.

As to mercury, the most varied drugs were combined with it with the object of increasing, extinguishing, preserving or lenifying its essential qualities. Aloes, litharge (lead protoxide), myrrh, sulphur, camphor, were the commonest ingredients used. Frequent use of opium, styrax, turpentine, olibanum, white lead, euphorbium, etc., was likewise in honour. But viper's fat, bear and badger's marrow, earth worms fried in oil or macerated in wine, frogs ground up alive, finally, and above all, human fat enjoyed a very high reputation, and gave with quicksilver a rich series of priceless products.

At the same time as mercury—sometimes usurping its place—physicians prescribed as local applications fumigations of orpiment (trisulphide of arsenic), gargles with alum, decoctions of roses and plantain, collutories with pomegranate wine, etc. For internal use they kept in stock large quantities of those famous confections which glorified the pharmacopœias of bygone days, namely, mithridate, diaphœnix, catholicon, and last,

but not least, that extraordinary complex composition theriaca, containing over seventy ingredients, and which in a simpler form was still to be found in some pharmacopœias half a century ago.

Theriaca must have been given fairly often to the syphilitic patients of the Hôtel Dieu of Paris, because it was held in great esteem in this establishment. At certain times of the year the hospital prepared the confection on a large scale and then notified the public of the fact; then the marvel was exposed to the public gaze before the principal portal of the institution. Here one of the apothecaries was stationed, who, in presence of a delegation of the hospital authorities, made known to the gathered throng the composition of the famous remedy and its admirable qualities.

China-root, sassafras, sarsaparilla and other sudorific remedies had also their partisans. But of all the exotic medicaments guaiacum certainly was the most celebrated, undoubtedly because—as the legend went—it had been discovered in the Occidental Indies by Gonzalve d'Oviédo, a Spanish gentleman who, unable to rid himself of his syphilis in Europe, went to America in search of a remedy. One of the most interesting accounts of guaiacum is given by Dr. Garcia da Orta in his book entitled, *Coloquios dos simples e drogas be cousas medicinais da India*, Goa, April 10th, 1563. The forty-seventh colloquy is given up to guaiacum, and as it is little known to medical historians I append some extracts.(2)

The wood of guaiacum from the time of its introduction into Europe enjoyed such extreme popularity that it well-nigh dethroned mercury. Physicians vaunted its supposed virtues as the only real specific of syphilis; merchants sold it as high as seven gold écus a pound, the people called it the *saint wood* and patients rendered thanks to Heaven, while poets of the time sang its praises to satiety. However, the enthusiasm at Paris was, perhaps, somewhat less because de Béthencourt, in his curious little book, gives precedence to mercury.

Physicians—eye-witnesses to the epidemic of the fifteenth century—looked upon syphilis as a new pathologic process, or at least unknown until then, and anyway quite distinct in nature from all other venereal affections—gonorrhœa, ulcus molle, etc.—which had been described since antiquity.(3) Now, little by little, probably on account of their similar ætiology, frequent coincidence and common character of contagiousness, the majority of these diseases became confounded and constituted a new morbid entity, clearly factitious, but in reality less serious than true

syphilis, since a group of exclusively local accidents destined spontaneously to subside and incapable of infecting the organism were included under the head of lues. These disastrous doctrines, which reigned in the Italian school from the time of Brassavola and Vella, were accepted at Paris by Le Cocq, Thierry de Héry, Pierre Deschampes and Fernel.

A curious thing and well calculated to prove that, even in the midst of the falsest systems, patient and rigorous observations alway bears fruit: while the nosography of syphilis went astray, the chapter of symptoms became daily enriched with strict truths and definite notions. The immense progress in the domain of syphilis realised in our days consequently must not allow us to lose sight of the fact that the majority of specific accidents —so familiar to all at present—were mentioned, if not to say described, by the physicians of the Renaissance. At the epoch when Fernel's famous work appeared the fundamental characters of syphilitic infection already were well known, its long incubation, the evolution of its periods, its continual metamorphoses, its long periods of latency and sudden outbursts, its congenital transmission, and, in a vague way, the para-syphilitic processes. It was perfectly well known that the primary lesions developed at the spot where contact had occurred, and that they were remarkable for their callous hardness. Fernel distinctly says that to become infected there must be an abrasion—although minute—on the mucosa or skin at which point the virus is absorbed.

There was not a barber-surgeon or charlatan sufficiently ignorant not to be able to enumerate the major symptoms of the disease, from the exanthemata and mucous lesions to the deep ulcers of the face, throat, and limbs. The nocturnal pains in the joints, muscles and bones, the headache, tubercles and gummata, the "squamous morphea on the palmar aspect of the hands and feet," the exostoses and caries, necrosis of the nose, ozæna and perforation of the palate were comprised in the group of common manifestations.

Syphilis of the liver, brain, trachea and œsophagus, specific lesions of the ear and syphilitic fever and cachexia are all described by the old authors. Nicholas Massa and Le Cocq refer to syphilitic adenopathies; paralysis and syphilitic epilepsy are clearly described by Thierry de Héry, whose book, *La Methode Curatoire de la Maladie Vénérienne*, is a gem, and well worthy to be read to-day, even although the first edition dates back nearly four hundred years. Had clinicians of the past few decades been awake to the knowledge of their sixteenth century *confrères*,

many of the discoveries dubbed "*modern*" would, in reality, be found to be very old.

Fernel also described specific alopecia. This lesion—unnoticed for a long time—suddenly assumed a surprising importance towards the end of Francis the First's reign. In 1546 Fracastor wrote: "For now almost six years the French disease has been undergoing changes. The pustules are scarcer, the pains lighter, but on the other hand gummata are relatively more common. Now, a very strange phenomenon occurs, namely, the falling of the hair, eye-brows and beard. This accident produces a ridiculous physiognomy in patients."

Up to the end of the sixteenth century alopecia or *pelade*, as it was then termed, made astonishing progress. Sauval, in his *Histoire et Recherches des Antiquités de la Ville de Paris*, tome ii, says, "Many persons became prettily shorn without the use of the razor." Thus King Henry III lost his hair. Alopecia became so frequent during syphilis that progressively this symptom was used to designate the entire disease. To say that somebody had the pelade became a too transparent metaphor not to be insulting.

With the exception of a few details the therapeutics of syphilis varied little during the sixteenth century. Mercury and the sudorifics continued to be in favour, and served unceasingly as a theme for professional disputes. For the majority of the public, for the bourgeois and the common people, mercury—in spite of its numerous opponents—remained the great antidote, and inunctions, strong or mild, were still preferred above all other methods.

When Master Antoine Le Cocq, an expert and erudite surgeon, but a mediocre courtier, received the invitation to give his opinion on the syphilis of King Francis I, he replied: "Frottetur, he is a vile person who has caught the pox; frottetur like anybody else and like the lowest of his kingdom, since he has tainted himself in the same manner." Although this declaration on the part of the eminent surgeon was somewhat hazardous as a preliminary statement, it was not in reality quite as severe as might be supposed, because the mercurial inunction had undergone very happy changes and was less severe than formerly. The barbarous procedures had been discarded which, according to the amiable periphrases of Thierry de Héry "went as far as to separate the soul from the body." Moreover, from this time on the art of selection began to show itself. Before making a choice of one of the various ways of

exhibiting mercury, the more serious-minded practitioners took into consideration the strength and temperament of their patients before beginning treatment; likewise the length of time the infection had existed, as well as the progress and seat of the lesions. Ambroise Paré distinctly says: "The way of curing pox, which is by inunction or friction, is the most certain and necessary treatment for this disease; but not invariably for all types (of syphilis) or their tendency, nor in all seasons."

I would merely mention mercurial plasters; fumigations of cinnabar (red mercuric sulphide), which were little used by the Paris profession, and then only in very severe cases; lotions of bichloride of mercury, extolled by A. Ferrier, physician to Catherine de Medicis; and lastly, urethral injections having metallic mercury as a base, fatefully introduced into therapeutics when gonorrhœa was annexed to syphilis.

But the event which, at this epoch, dominates the entire history of mercury was the vulgarisation of its internal exhibition. At first the suggestion caused much excitement. The fervent disciples of the Galenic dogmas persisted in maintaining, on the faith of the oracle, that mercury was a violent poison, and in this respect they invoked Dioscorides, who states in his chapter on quicksilver that when taken internally it undermines and erodes on account of its weight. But to Galen's anathema the innovators replied that the physician of Pergamos never had experimented with mercury, and that he admitted this himself in his *Treatise on Simples*. To Dioscorides they opposed Avicenna; to those who maintained that mercury eroded and perforated the intestine they quoted the observations of Jehan de Vigo and Mattioli. Most of them even went so far as to base their opinion on the extraordinary tales of Marianus Sanctus and Antonio Musa.

Consequently syphilitics were treated by the internal exhibition of mercury. Under the name of *angelical powder* red precipitate was the first mercurial salt given *per os*. Later on crude mercury was preferred. Thus it was the ingredient of the famous pills that Barbarossa, King of Algiers, is said to have sent his ally, Francis I. But the pills of the good Barbarossa, which wrought wonders with the Turks, did not have the same success in France. It was noised about that the first Christian who had dared to take one fell dead on the spot—a tale that gave food for thought to many patients. Then the angelical powder became popular again. Nevertheless, in 1560, crude mercury was again in use under another label, in the pills devised by Rondelet, professor at

Montpellier, and it can be said that since then pills of metallic mercury have always enjoyed a large place in the pharmacopœias of every country.

As the guaiacum and other sudorifics they appear to have lost their prestige at a relatively early date. Towards the end of his long career Thierry de Héry declared that he had never seen a case of syphilis thoroughly cured with only decoctions of the wood, and he esteemed that sudorifics were merely of use as auxilaries to mercury. A large number of physicians and surgeons of Paris were of like opinion.

Thierry de Héry, whose erudition was known to the profession at large in the sixteenth century, in his youth had been an aid-barber at the Hôtel Dieu of Paris, as had been Ambroise Paré and a host of other well-known surgeons of the time. Later on he practised his profession as an army surgeon, afterwards going to Rome, where he studied for a long time at Saint James the Major Hospital, which was noted in those days for the treatment of venereal disease according to the rules laid down by Berenger di Carpi.

After his return to Paris, de Héry soon became known by many successful cures, and made a very large fortune for the times. Of his book, the first edition of which appeared in 1552, I have already spoken. *À propos* of his fortune, the following anecdote has been related. One day de Héry visited the basilica of St. Denis and was in the act of kneeling before a royal tomb when a monk came to him and said: "Rise, my brother, it is King Charles VIII who sleeps under this slab, and one must only kneel to saints." Whereupon the surgeon replied: "I am well aware of that, but I have a very special devotion for Charles VIII, because by importing pox from Italy into France he made my fortune."

Mr. President and Gentlemen,—I am fully aware that I have not given you any new documents relative to the history of syphilis, and I have also abstained from entering into the nebulous discussion on the European origin of this disease. My object has merely been to sketch as faithfully as possible a picture of the greatest scourge that has ever afflicted humanity during the first two centuries of its existence, and selecting as scenery the Paris of the Valois, that our distinguished *confrère*, François Rabelais, found to be "une bonne ville pour y vivre."

(1) Note A.—"That syphilis has existed from the earliest times in Asia is an old belief which some modern controversialists like Bloch have vainly attempted to discredit. Internal evidence, such as vernacular terms for various ailments, seems to show that there have always been in use certain designations. Even if

the diseases themselves are new, the names, as applied to diseases, are old. With these names may be associated certain beliefs, folk-lore, etc., showing a common suggestiveness among ancient and modern peoples. There are also archæological evidences of excavation finds. Dr. Christidi, of Constantinople, who has studied syphilis and leprosy among the Persians (*La Presse Médicale*, March 15th, 1922), believes that the former has prevailed in that country, like leprosy, from very early times, at least as far back as the days of the Phœnician merchants, who, as the only commercial travellers of the period, were able to disseminate the infection. There is an ancient Persian anathema, 'kouft, equivalent to our 'pox' and similar expletives, which, as the native word for syphilis, speaks volumes. The collections of old terra-cotta in Persia—images with certain inscriptions—speak for the existence of a disease with such symptoms as sore mouth, snuffles, severe headache, etc. These exhibits the author has personally studied. Moreover, there was confusion between syphilis and leprosy, as happened also in mediæval Europe. Some descriptions of leprosy apply clearly to both diseases. The same confusion exists to-day in the minds of the empiric physicians of Persia. The author cites a very ancient manuscript, the source of which is not stated, save that the original antedates the Christian era by several centuries. The manuscript of the present day is a copy in Arabic which goes by the name of the 'Bouquet of Medicine.' It speaks of two forms of leprosy, one acute and contagious in evolution, the other much more chronic and but slightly contagious. The acute contagious form answers to syphilis.

"Persian syphilis, considering that there is no evidence of any common successful plan of treatment, is on the whole relatively benign. If this was not originally the case—and the use of the expletive 'kouft' would seem to indicate that it was once a scourge—it has evidently become so through saturation of generations of Persians. Mercury is in use to-day, and has been for years past, but not treatment as we understand the term. To-day only one in fifty gets a prolonged and thorough medication. Innocent transmission is very common, just as in Russia. When a European contracts the disease from a Persian woman the course is usually benign. The author noted some severe cases of the disease in which the woman in the case was not a Persian, and in two of these cases paresis developed. The nationality of these foreign women is not stated. The author saw at least 3000 cases of syphilis in Persia, and, in general, Persian syphilis sufficiently resembles the European, with some notable differences. He saw no metasyphilis in native Persians, but, singular to relate, there seemed to be a well-defined syphilitic epilepsy which was present in hereditary cases and most commonly in women."—*Editorial, Medical Record, April 22nd*, 1922.

(2) NOTE B.—*Extracts from the Forty-Seventh Colloquy: Root of China.*

"*Ruano:* I want to take back with me to Portugal some of the root or stick of China. . . . Will you describe to me its appearance and for what illnesses it is serviceable? . . . I also want to know . . . which is the best—this or the *Guaiacam* of our so-called Indies? . . .

"*Orta:* This stick or root grows in China. . . . As all these lands (eastern India) and China and Japan have this *morbo napolitano*, it pleased a merciful God to provide this root as a remedy with which good doctors can cure it, although the majority fall into error. . . . Now, Sir, I have reason to hold that this *guaiacam* is better than the root of China. It is certain that the

other is efficacious, given with reference first to the quality and character of the patient, then to the nature of the illness, the season, the country, the heat, the cold, the sex and age of the person who takes it. Be not surprised that I praise it, for I have heard no one else praise it, so many writers praising the *guaiacam* every day. Among them is a German writer who composed a book on his labours in a very copious style and very pure Latin, which might all have been written on one sheet of paper. Of this other root of China, Vesalio and Laguna say many evil things. . . . I do not care whether it costs much or little, . . . but I consider what Mateolo Sinense says to be good—that it is sufficient proof that this medicine is valuable that the Emperor Charles V took it and benefited by it.

"*Ruano:* In using *guaiacam* we always give salt, because it is an enemy to arid humours and inflammations. Many men have told me that they also give it, but I do not know how they would use salt with this root.

"*Orta:* Salt may be used moderately, for it is not necessary to be very exact in physic, leaving much to the good judgment of the physicians. I think that the use of a little salt cannot do any harm to the arid humours, nor salt to inflammations, for I have always done well in using it. . . .

"*Ruano:* . . . For what illnesses is it (China root) found efficacious?

"*Orta:* For any infirmity connected with *morbo napolitano* or for humours engendered by it. It is also good for paralysis and for shivering fits, of which I cured Nizamoxa with it in a short time, for arthritis, exema, sciatica, gout, scrofula, indigestion, swellings produced by melancholy or by white tumours, old hurts, stone and ulcers of the bladder sometimes, for with this root the stone is got out which never could be removed before. . . ."

(English translation by Sir Clements Markham, K.C.B., F.R.S., London, 1913.)

(3) NOTE C.—The early writers on syphilis did not connect gonorrhœa with syphilis. It was at a much later period than this error was committed, so that during the eighteenth century the two morbid processes were regarded as one in all countries, as will be seen by the following definitions from the text-books of the time.

"Post impurum concubitum ulcuscula, porri, bubones, fici primo ut plurimum in genitalibus, prægressa non raro gonorrhœa, dein pustulæ crustosæ, dolores nocturni, exostoses, caries, etc., in cæteris partibus."—*Sauvages (France).*

"Cachexia contagiosa, ex contagio venereo, cum tumoribus ossium et ulceribus faucium, partiumque obscænarum, prægressis plerumque bubonibus aut gonorrhœa."—*Vogel (Germany).*

"Ulcuscula, porri, ficus, bubones, tophi, nodi, post vel cum gonorrhœa plerumque; dein pustulæ crustosæ, dolores nocturni osteocopi, exostosis, caries, macies et calor luridus, morbum adesse loquuntur."—*Sagar (Poland).*

However, towards the end of the eighteenth century the profession had begun to suspect that gonorrhœa and syphilis might be two distinct processes, as is clear from the statement made by Aitken in his *Elements of Physic and Surgery*, vol. ii, p. 187, London, 1783, to wit: "It has been supposed that the poisonous matter generating clap is specifically different from that which is capable to produce general syphilitic affection, because this last is not often connected with the former. The possibility of both being caught at once is a fact perhaps eversive of this distinction."

"FORME FRUSTE" OF V. RECKLINGHAUSEN'S DISEASE (NEUROFIBROMATOSIS DISSEMINATA MULTIPLEX).*

KR. GRÖN,

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Translated from the Norwegian by W. JENKINS OLIVER.

THE patient, O. B—, a bookbinder, aged 36 years, was admitted to the Skin Department of the Ullevaal Hospital on October 10th with ulcerations on the legs. The details of his previous history, obtained with difficulty, revealed that when two years of age he had what was called inflammation of the brain, following which he became paralysed in the left lower limb, and had pains in the back; at any rate there is now developed, as a result, a definite scoliosis at the lowest part of the dorsal column with the convexity towards the right side; at the same time the vertebral column is slightly twisted on its long axis. In consequence of the above quoted trouble he has latterly been practically an invalid; as a child he had to drive to and from school, where he reached only the third class; during the last six years he has been quite unable to do any work. During the last year he has had swelling and ulceration of both legs. The feet are deformed, the left showing pes equino-varus. There is increased mobility of the talo-crural and toe joints, lowered sensibility in the lower extremities, and increased knee-jerks. On the lower limbs the skin is thin and soft like a child's. At the present time the ulcerations on the legs, noted on admission and of annular progression, are now healed. W. R. negative October 12th, 1922. On examination of the back there is found on the lowest part of the right side a soft elastic tumour, in size about that of a hen's egg, somewhat sharply defined and slightly tender on pressure, over which the skin is rather hyperæmic and is covered with some few hairs; on more careful palpation several smaller subcutaneous nodules can be recognised, over which the skin is of normal colour. Just to the inner side of the large tumour is more specially to be noted a linear band-like growth, about 3 cm. in length, which at its most posterior limit shows a slight nodular thickening. A little below the costal margin on the right side there may also be felt a smaller nodular growth. On the

* Communicated to a meeting of the Ullevaal Medical Association, November 10th, 1922.

right side of the abdomen there are some pigmented skin lesions (nævi pigmentosi) from size of a pea to that of a Brazil nut, and on the left side of the chest one single oat-sized angioma.

In its ordinary form v. Recklinghausen's disease is well known. While first described in 1835 by Rayer we are indebted for a more detailed description of it to v. Recklinghausen (Strasbourg), who in a "Festschrift" to Rudolf Virchow in 1882 wrote a monograph entitled "Ueber die multiplen Fibrome der Haut und ihre Beziehung zu den multiplen Neuromen." The disease is not so rare; a monograph of 1901 counted up 360 publications to that date; Harbitz (1909), in his paper on "Tumours in Nerves and Multiple Neurofibromatosis," considered that there had been described in all about 500 cases—a figure which might now undoubtedly be doubled.

The fully developed condition shows the well-known triad—skin tumours, pigmentation and teleangiectases. Basing my remarks on this reported case I am anxious to lay particular stress upon the fact that of this skin disease, as of so many others (for example psoriasis, zoster, dermatitis herpetiformis, etc.), there may certainly occur incomplete or abortive forms, and that such types of the disease are indeed not so uncommon if one is on the look-out for them. I am quoting here Harbitz's article already mentioned (*Norsk. Mag. f. Lægev.*, 1909, Nos. 2–4). During the last two years in my skin department I have seen two further cases of this kind. It is only comparatively recently that attention has been drawn to these incomplete forms of the disease, of which one now finds mention fairly often in dermatological literature. In a monograph by Alexis Thomson "On Neuromas and Neurofibromatosis" (Edinburgh, 1900), regarded as a classic, there is no mention of them. In England, Parkes Weber was, I believe, the first to describe the condition in his "Cutaneous Pigmentations as an Incomplete Form of Recklinghausen's Disease, with Remarks on the Classification of Incomplete and Anomalous Forms of Recklinghausen's Disease" (*British Journal of Dermatology*, 1909, p. 49). He drew special attention to the occurrence of undoubted cases of neurofibromatosis with typical excessive cutaneous pigmentation, although practically without any superficial growths. Somewhat about the same time Cecil Reynolds reported "A Case of Multiple Plexiform Neuromata associated with Brown Pigmentation of the Overlying Skin" (*Brit. Med. Journ.*, 1909, ii, September 16th, p. 745), touching on the same question. In 1915 Scholl (Strasbourg) emphasised the same point

in a dissertation, "Ueber abortive Formen der Recklinghausenschen Krankheit."

The above-mentioned writers all adopt the same point of view, which might easily be supported by similar examples from later years' literature —that the pigmented lesions may appear either a shorter or longer time before the development of tumours. Weber quotes several cases of neuro-fibromatosis in which definite pigmentation had occurred a long time before the neurofibromata on the nerve-trunks or mollusca were noted. In his own case, that of a girl, aged 14 years, the pigmented patches had been present since the age of 18 months. These consisted of (i) diffuse brown coloration over the back and neck, (ii) small brown spots over the whole trunk, (iii) a dark pigmented nævus on the left side. In May, 1905, there had been only the pigmented lesions and one single tumour, while by July, 1908, several pendulous mollusc-like tumours had developed over different parts of the body. Reynolds' patient was a little girl, aged 5 years 4 months, who had one tumour over the greater part of the neck stretching downwards from the uppermost limit of the occiput to the top of the first dorsal vertebra, and laterally to the anterior edge of the left sternomastoid muscle; the skin over the whole tumour with the exception of that part over the occipital area showed the pigmentation, most marked over the neck region. He draws particular attention to the fact that the brown pigmentation had been observed when the child was 2 years of age, while the growth had been noticed to commence one year later at the upper part of the pigmented skin. This tumour on operation had proved to be a plexiform neuroma. In one of Scholl's patients, a girl, who first had shown only pigmented patches, the typical skin tumours developed during the time that she was under his observation.

It is only very rarely that a typical neurofibromatosis appears as a congenital condition; usually the characteristic signs first declare themselves at a somewhat later age, occasionally during childhood, more frequently during early puberty, to later become more and more extensive. It has been well known and for so long a time that neurofibromatosis is a family affection that it is unnecessary for me to labour that point now; in Harbitz's often quoted article is one case recorded where the disease could be traced through five generations. Many examples of a similar hereditary disposition are to be found in the literature.

However, there are some newer theories concerning the pathogenesis

of the disease which I shall shortly mention. The view most generally held now is that the development of skin tumours in cases of generalised neurofibromatosis is only one sign of the disease, possibly the most palpable, but perhaps rather a secondary one, while the pigmented nævi appear certainly to play an important part. The older theory of Feindel (1896) that neurofibromatosis is a disease of the ectoderm is partly opposed to that of Verocay (1910). The latter believed the tumours to be due to a congenital disposition to the disease, dependent upon an early embryonal disturbance in development of the specific elements of the nervous system, which disturbance might have affected cells that were on their way to produce ganglion. glia or nerve-fibre cells. Now, however, the general opinion may be said to be that the mesodermal elements are chiefly concerned. With regard to the disease as a whole, there is a growing tendency to place it in association with affections of the endocrine system (of the suprarenal, pituitary and thyroid glands); these latter may be primary, or, as Ehrmann (Vienna, 1921) considers, may be due to a displacement of the secretory parenchyma by the neurogenous tumours. In the recent literature there are reports of cases of Recklinghausen's disease which on post-mortem examination have shown lesions in the suprarenals (most recently reported case is that of Chauffard and Brodin in *Société médicale des hôpitaux*, 1920). Ormond (*British Journal of Dermatology and Syphilis*, xxxii, p. 345, 1920) and Escher (*Annales de dermatologie et de syphiligraphie*, 1922, No. 1) reported cases of Recklinghausen's disease with acromegaly. From two sources there are reports of a simultaneous occurrence with adenomata sebacea which are known to be associated with sclerosis tuberosa cerebri—an idea first conceived by Bourneville in 1880; on the other hand, it is maintained by Carol of Amsterdam (*Acta dermato-venereologica*, ii, p. 2) that adenoma sebaceum does not occur with Recklinghausen's disease.

In addition there occur dystrophic symptoms, mentioned indeed by Harbitz (*loc. cit.*), though he does not lay much stress upon them; still, they appear so frequently in the recent literature that one particular writer (Engman) even considers such signs as constant. In the case which I have here reported there was kypho-scoliosis, which condition according to an American writer—Richard Weiss—is associated with endocrine disturbance.

A theory also to be mentioned, rather as a curiosity, is that of Ludwig Merk (Innsbruck). In two articles in *Med. klinik* (xxxi, 1920, and xxxii,

1921) he upholds what he calls the botanical nature of Recklinghausen's disease. In the skin tumours he had found vegetable bodies (parenchyma cells, crystals, spiral vessels, etc.), which must, he believes, have developed in the growths themselves. He further is of the opinion that the plant which in man grows in the form of a tumour has preserved from its previous free existence the property of secreting to some extent its customary metabolic products in the human subject. The theory is based mainly on microchemical examinations. Merk found that sections of tissue from the tumours in Recklinghausen's disease treated with pure concentrated sulphuric acid showed a peculiar bluish violet staining, which gradually became paler, to disappear in a few hours. This peculiar staining was foreign to the action of connective tissue and nerves, but pointed towards the vegetable kingdom. Merk considers that he has found a similar reaction with tumours of adenoma sebaceum and with sclerosis tuberosa cerebri (*cf.* above references).

Henneberg (*Berl. klin. Wochenschr.*, 1921, No. 17) had in one single case of neurofibromatosis observed fully developed gastric crises as in tabes. Harbitz (*loc. cit.*) mentions cases of the disease which recall to mind the temperature crises sometimes occurring in tabes. These observations indicate a combined affection of the central nervous system. On post-mortem examination of patients with neurofibromatosis there are indeed frequently found various collections of cells in the central nervous system, particularly in the medulla spinalis. These deposits may possibly be sometimes connected with the metameric forms of neurofibromatosis, as in zoster.

Frequently there is an accompanying mental weakness, but this is by no means constant. Nardi has found such a case recorded where the neurofibromatosis, without any hereditary or congenital disposition, had developed in a girl of 17 years as a sequence to melancholia and nervous instability induced by unhappy family circumstances.

In conclusion a few remarks on treatment. In my department we have once had the opportunity of using salvarsan upon a case of neurofibromatosis with syphilis, but without any effect upon the tumours. Ludwig Kenez (*Deutsche med. Wochenschr.*, No. 3, 1917) has obtained a definite cure in a case of multiple neurofibromatosis with 22 injections of fibrolysin spread over a period of two months. I have also tried this preparation in one case, and the patient in question appeared to show a slight involution of the tumours, but this, however, is not so infrequently a spontaneous occurrence.

CLINICAL NOTE.

TREATMENT OF PARAPSORIASIS.

C. RASCH.

Translated from the Danish by W. Jenkins Oliver.

The patient, who was demonstrated before the Danish Dermatological Society in March, 1923, was a girl, aged 15 years, from the country, who first attended the University Dermatological Clinic at the Rigshospital on January 4th, 1923, for a skin disease which had commenced six months previously. The patient was well developed, and on examination showed nothing abnormal with the internal organs. Menstruation had commenced about six months earlier, at about the same time as the skin affection was first noticed. The eruption had first appeared on the arms and legs, and had later spread over the greater part of the body under treatment with different ointments.

On admission there was found an almost generalised affection of the skin, consisting in the formation of macules and papules—a wide-spread reticular pattern of scaly atrophic puckered macules, such as occur in typical cases of parapsoriasis. Only in occasional places were the scaly papules arranged in rings. The affection was most marked on the lower limbs, and here in several places closely resembled psoriasis. There was a pronounced acrocyanosis of all four extremities. Pirquet reaction +. Since I had noticed on several previous occasions that parapsoriasis was very easily made worse by external treatment (which I was able to record in my two first cases reported to the Society in February, 1914), in this case I withheld any form of local treatment, and only prescribed for the patient calcium chloride internally (sol. calcium chloride, 20–300 grm., 15 grm. five times daily). The result was that the disease had completely disappeared by February 14th, and she remained clear during the three following weeks to the time of demonstration.

The improvement, which took place slowly and regularly, could be already observed ten days after the commencement of the treatment. That this progress was not due to any coincidence, but was the result of the treatment adopted, I consider as practically certain, since two other cases occurring in my private practice and treated after the same manner reacted in the same way. I am, however, somewhat doubtful as to

whether the effect produced was due to the calcium chloride, or solely to the fact that the skin was not irritated by any external application. According to my own observations I am inclined to believe that the disease can be kept up by a steadily maintained local treatment, and that it is just this circumstance which occasions its long continuance. Occasionally also a spontaneous cure is observed.

Instead, therefore, of defining parapsoriasis as a papular, scaly and chronic disease, resistant to therapeutic measures, as many dermatologists do, for my part I have been led to think that, in some cases at least, it may be called a subacute disease, which may easily be made a chronic one by intemperate and irritating local treatment.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

Meeting held on May 17th, 1923, Dr. H. G. Adamson, President of the Section, in the Chair.

Dr. Aldo Castellani showed a case of *peculiar folliculitis of the scalp*. He showed the patient at the April Meeting, when the condition was in a much more acute stage. A number of different diagnoses were suggested: a syphilide, folliculitis decalvans, ordinary pyogenic folliculitis, lupus erythematosus, even favus. At that date he was not in a position to make a definite diagnosis, but during the intervening four weeks he had gone into the case pretty thoroughly, and would give the results of his bacteriological examination. The first symptoms started eighteen months ago, and the patient was treated by a practitioner who diagnosed staphylococcus infection; he sent specimens to various laboratories, the reports from which were always to the effect that staphylococcus was present. Therefore a staphylococcus vaccine was prepared, and he had had that administered to him off and on for the last twelve months, but without improvement. The result of the exhibitor's complete bacteriological examination was the following: There were a large number of staphylococci in stained preparations and on cultivation, but he succeeded in growing also a fungus, which was either a torula, a cryptococcus, or a monilia. It did not produce gas in any sugar. The cultures after a time often presented a peculiar yellowish-brown pigmentation. He had little

doubt that the principal part in causation of the condition was played by the fungus, and this was confirmed by the patient having been treated with a staphylococcus vaccine for twelve months without benefit. As soon as he found the fungus he put the patient on potassium iodide and a vaccine prepared from the fungus was administered, and they would now see the result. The condition of the scalp was certainly much better than a month ago.

Dr. Aldo Castellani showed a case of *trichomycosis axillaris rubra*. The patient had been under his care for dysentery and other complaints for nearly two years. It was a typical case of trichomycosis rubra, which he appeared to have contracted in this country, though he was in North Africa ten or twelve years ago. He noticed this discoloration only a year ago. Trichomycosis rubra was very rare in this country, but it was common in the Sudan, in India, and Ceylon. Some years ago he separated three forms of trichomycosis axillaris—trichomycosis flava, trichomycosis rubra, and trichomycosis nigra. The first of these was the variety usually found in this country. It was caused, according to his view, by a minute bacillus-like fungus, *Nocardia tenuis*. The black variety was caused by the same fungus plus a black pigment-producing fungus—*Micrococcus nigrescens*. Trichomycosis rubra was caused by the same fungus plus a red pigment-producing coccus—*Micrococcus castellanii* (Chalmers and O'Farrel). Trichomycosis rubra and trichomycosis nigra were interesting examples of symbiosis; they were conditions due to two germs, a fungus and a coccus, growing together. Further particulars on the various types of trichomycosis axillaris might be found in his recent paper on the condition in the *British Journal of Dermatology*, vol. xxxiv, August-September, 1922, pp. 255–266.

Dr. H. W. Barber showed a case of *dermatitis repens and infectious eczematoid dermatitis, with involvement of the mucous membranes*. The patient, a male, aged 58 years, had periodically suffered from boils and carbuncles, which had always quickly yielded to treatment. About three months ago he developed a whitlow on his right thumb, which was opened by his doctor under gas; following the operation an eruption appeared near the base of the nail, and spread up the thumb, the horny layer being stripped up and a raw moist surface exposed. Later, other parts of the right hand became involved and the eruption also appeared on the left

hand, on the penis and scrotum, on the forehead, and on the feet and legs. He also developed an acute discharge from under the foreskin, also acute conjunctivitis, and stomatitis.

He was referred to Dr. Barber by Dr. Flynn on April 11th, 1923. At that time he had typical lesions of dermatitis repens on both hands and feet, an acute eczematous dermatitis of his penis and scrotum and behind the ears, a scaly eczema of his forehead, conjunctivitis and superficial glossitis and stomatitis. There was a profuse purulent discharge from under the foreskin, and a slight one from the urethra. He was admitted to Guy's Hospital on April 19th, 1923. By that time the conjunctivitis had subsided, but the eruption had spread on to the forearms and legs in the form of pustules and eczematous lesions. The lesions on the palms and soles superficially resembled those of keratodermia blenorrhagica. The patient was examined by Mr. V. E. Lloyd, who reported that there was acute balanitis and slight urethritis, but he thought that the urethritis was not due to the gonococcus.

Mr. E. Biddle, Chief Assistant in the Bacteriological Department, made the bacteriological investigations. Cultures of the skin lesions on the palms and soles, legs, forearms, penis and scrotum all gave a pure growth of a *Staphylococcus pyogenes aureus*. The same organism was also recovered in pure culture from the urethra, from the pus exuding from under the foreskin, and from the urine. Smears from the urethral swabs and from the urinary deposit showed no gonococci.

The patient's blood-serum tested against his own staphylococcus gave agglutination in dilutions of 1 in 20 and 1 in 200.

The complement-fixation tests were as follows: Gonococcus, *positive*; autogenous staphylococcus, *strong positive*; stock staphylococcus, *strong positive*.

The Wassermann reaction was negative.

An autogenous staphylococcal vaccine was prepared, and an initial dose of 25 million was followed in twenty-four hours by an acute spread of the eczematous dermatitis in the groins. His condition was now much improved and further vaccine treatment was being cautiously continued.

This case resembled those originally described by Crocker as "dermatitis repens," and Hallopeau as "acrodermite continue," although Hallopeau did not consider that his cases were identical with Crocker's. Sutton, in 1911, described three cases and gave histological descriptions, and he came to the conclusion that the cases of Crocker and Hallopeau were of

the same nature. He cultivated a *Staphylococcus aureus* which he considered to be the causal organism.

Dr. J. H. Stowers confirmed Dr. Barber's diagnosis and said that this disease was of rare occurrence. He referred to a typical and severe case, which he published in the *British Journal of Dermatology* in 1896, with coloured plates, and which was exhibited at the Dermatological Society of London. The patient, a married woman, aged 67 years, was sent to him by Dr. Reid, of Canterbury. In this case no history of injury could be obtained, but the disease commenced in 1888 within a fortnight of the birth of her last child. The primary lesion, described as a small "gathering," occurred in the matrix of the right thumb-nail. The nail became loosened and detached by inflammation. The ulceration never healed, but the left thumb, and all the fingers of both hands, became similarly involved at intervals of several months. Subsequently the nails of all the toes became affected, and the inflammatory and ulcerating process gradually spread up the whole of the hands and the distal half of each foot. The disease had been defined as a spreading dermatitis usually following injury, probably neuritic, and commencing almost exclusively on the upper extremities. The late Dr. Radcliffe-Crocker, who was the first to describe the affection and who had already recorded two or three cases, saw the patient and confirmed the diagnosis. In addition to these, similar cases had been recorded by Charlton and Coward in this country, Garden, of Aberdeen, and Hallopeau, Frèche, Audry and Carle on the continent. The disease, always very rebellious to treatment, might ultimately yield to local remedies of an antiseptic nature, but internal treatment appeared to have no beneficial effect. He (Dr. Stowers) treated his case with a lotion of permanganate of potash as suggested by Dr. Crocker, but, later, continuous application of the 5 per cent. oleate of mercury appeared to produce a better result. The patient did not recover, and ultimately died of an intercurrent disease.

Dr. H. G. Adamson (President) said that Dr. Barber's case showed many features which suggested psoriasis: for example, the sharply-margined patches with scaly surface, and on scraping some of the lesions the same appearance was left as in psoriasis. The patient might have psoriasis with a secondary infection.

Dr. Barber, in reply, said that although the patient had recently developed patches which looked like psoriasis, he (the speaker) did not entertain that diagnosis, as there was an acute involvement of the mucous membranes, and the greater part of the eruption was quite unlike psoriasis.

Dr. H. W. Barber showed a case of *atrophic dermatitis of the hands and feet; ? lupus erythematosus.* The patient, aged 51 years, female, was admitted under Dr. Beddard to Guy's Hospital on May 2nd, 1923, for breathlessness on exertion and swelling of the feet. She had suffered from breathlessness on exertion for the past fifteen years, but the swelling of the feet had only occurred during the previous ten days, and was most marked in the evening. During the last ten years the skin of the fingers and toes had become bluish in colour and very thin. The nails had also

atrophied and had almost disappeared. The changes in the fingers and toes had not been accompanied by pain or ulceration, nor was there a history of "dead" fingers such as one obtained in cases of Raynaud's disease. Dr. Beddard diagnosed senile emphysema, slight sclerosis of the mitral valve and myocardial degeneration.

Dr. Barber was asked to see her on account of the condition of her hands and feet. The skin of the fingers and toes was bluish red and atrophied, and the nails had almost disappeared. The appearances were not unlike those seen in lupus erythematosus of the extremities, but there had never been any eruption on the face, ears or scalp.

The Wassermann reaction was negative.

He wanted to raise the question as to whether this case came under the heading of those described on the Continent as acro-dermatitis atrophicans. The appearance of the fingers suggested to him lupus erythematosus, which he had seen with nail changes.

Dr. H. C. Semon showed two cases from *an outbreak of alopecia occurring in an orphanage.*

The first child, aged 8 years, had been an inmate of the orphanage fourteen months, and entered it with typical alopecia areata. On April 27th it was noticed that she had a bald area on the right frontal region. On May 3rd the second child shown was noticed to have a bald area on the left frontal region, *not* typical alopecia areata. Most of the heads in the institution were examined, and fourteen had a similar condition of a typical alopecia. The patches were not round, but of angular outline, and not completely denuded of hair, and showed no typical comma-shaped stumps. They were therefore here dealing either with an epidemic of unknown ætiology, or, as had been suggested by French writers, with an artefact condition. Dr. Haldin Davis described an epidemic, also in a girls' asylum, in 1914; and Bowen, whose paper in the *Journal of Cutaneous Diseases* for 1915 was worthy of study, had described this peculiar condition as occurring in another girls' school.

Dr. J. H. Sequeira thought it most likely that these were cases of imitative artefact.

Dr. Haldin Davis said he had seen an almost exactly similar epidemic in a home for children in 1914; and, several years afterwards, he concluded it must be imitative artefact. At the time he first saw it he wondered whether any of the children had cut their hair, but concluded that they did not do so. But subsequently he formed the opinion that having had their attention directed to

the scalp, they rubbed it with their forefinger, which soon broke hairs off Another cause of the epidemic in that institution was that nurses and attendants were very assiduous in searching the heads of all the children to find something, and conditions which in the ordinary way would pass unnoticed were, under these conditions, made much off.

Dr. O'Donovan said he had come across a parallel epidemic in Dr. Sequeira's clinic; there were five cases brought from an institution which at first seemed to be tinea capitis. In the first of the five the spores were obvious; in the others there were bald patches and some short hairs, but several examinations failed to reveal anything. A casual remark was made by an accompanying attendant that "boys were devils," and it transpired that the boys, seeing what interest was aroused by a case of ringworm, dropped sealing-wax on one another's hair and then pulled the stumps out. In New Bond Street there was exhibited for sale a wax which was melted and applied to unwanted hair, which afterwards could be removed *en masse*. He had a case of autophytic baldness—a youth with bad asthma who, between his spasms, sat up in bed and plucked at his frontal hair. After the attacks he dyed his temporary bald patches with a solution of permanganate of potash. A parallel case of autophytic alopecia was that of a very neurotic old woman with great trouble at home, who clipped large areas off her scalp and sought advice at the clinic for the resulting baldness.

Dr. Graham Little showed (1) A case of *lupus erythematosus;* (2) a *case for diagnosis;* (3) a case of *extensive urticaria pigmentosa nodularis in an infant.*

Dr. J. H. Sequeira showed a case of *tuberculous lymphangitis of skin.* Patient, a female, aged 55 years, had had lupus vulgaris of the atrophic type on the face for seventeen years. Eighteen months ago she developed a sore between the right first finger and the second, and following upon that there developed rather rapidly an acute swelling of the forearm and arm—a swelling approaching a pseudo-elephantiasis. On this, which he thought was the result of tuberculous lymphangitis, there had developed a large number of nodules, standing up about $\frac{1}{8}$ in. above the surface. Histologically their surface had been found to be tuberculous. The nodules on the back of the hand and across the back of the wrist were of that type of lupus which at one time was called lupus hypertrophicus. He had not before seen so marked a case in the upper limb, but he had had several in which the lower extremity had been affected, and this had always been associated with the direct inoculation of the skin, which had been followed by lymphangitis. Improvement was very slow. This patient had not yet had any treatment, but he hoped to show her at a later date.

Dr. A. M. H. Gray showed a case of *acne scrofulosorum.* The patient, a female child, aged 6 years, was admitted to the Hospital for Sick Children,

Great Ormond Street, under Dr. Still. She had had the eruption two years, and it had been associated with bilateral swelling of the wrists, knees and ankles. The eruption was of interest from several points of view. It consisted of indolent follicular pustules of the acne scrofulosorum type, which occurred chiefly on the extensor aspects of limbs, a few scattered lesions on the back, and very marked lesions on both cheeks. On the extensor aspects of the limbs there were larger lesions, varying in size from that of a threepenny-piece to one 6 in. in diameter on the leg. She also exhibited a curious condition of scalp, in which there was, apparently, nothing very active, but which closely resembled folliculitis decalvans. The joints noted above were still swollen. There were signs of tuberculosis at the left apex. She gave a negative Wassermann but a strongly positive von Pirquet reaction to both human and bovine tuberclin. There was no recent tuberculosis in the family, nor any history of it. He thought there could be no doubt that the larger patches were formed by the aggregation of the follicular pustules: in some of the small ones they could see acne scrofulosorum patches arranged round the main lesions. There was also no evidence of lupus nodules in these larger patches. Sections showed a granuloma of the tuberculous type, but tubercle bacilli could not be found. The lesions on the face were, he believed, a true example of Barthelemy's "acnitis," and it would be observed that they bore no resemblance to Crocker's "acne agminata" nor to Boeck's "miliary lupoid." The scalp condition was apparently of the same nature as the rest of the eruption, and it so closely resembled a "folliculitis decalvans" as to raise the question whether this latter condition might not possess a possible tuberculous ætiology. He had not seen this suggestion made.

Dr. S. E. Dore thought the case important; the association of what appeared to be folliculitis decalvans with tuberculides seemed to be unique. He asked whether folliculitis decalvans ever occurred in children. He thought the scalp condition was part of the tuberculosis due to the same condition as the eruption on the skin.

Dr. J. H. Sequeira said he hoped the case would again be shown before the Section, as he believed that this scalp condition associated with tuberculides was unique.

Meeting held on Thursday, June 21st, 1923, Dr. H. G. Adamson, President of the Section, in the Chair.

Dr. E. G. Graham Little showed a *case for diagnosis*; ? *papulo-*

necrotic tuberculides. The patient was a girl, aged 16 years, over-fat, with a chilblain circulation and an unhealthy colour. The exhibitor suggested as a tentative diagnosis papulonecrotic tuberculide of an acneiform type. The history was very curious: She had had four attacks of measles in six years, the last attack being in 1912. Twice in 1915 and 1916 she had had an eruption diagnosed as scarlet fever and she had had an attack of jaundice eighteen months ago. The present eruption appeared about a fortnight ago; it came on fairly acutely, but she seemed to have had similar attacks previously, though the history in this respect was rather indefinite. The eruption consisted principally of hard shotty papules with a minute central pustule. It was thickly distributed on the forearms, less thickly on the dorsum of the hands. There was no itching. On both upper arms just below the shoulder there were some areas of grouped follicular papules which were almost certainly examples of lichen scrofulosorum. The patient's father told him that up to two years ago she was very thin and anæmic, and had become very fat only within the last few months. This plumpness he took to be the *faux embonpoint* which the late Dr. Pringle used to point out as being typically tuberculous. There did not appear to be any other symptoms of tubercle at the present time.

Dr. H. C. Semon showed a case of *xantho-erythrodermia perstans* (*Crocker*). *parapsoriasis en plaques* (*Brocq*). In his article in the *British Journal of Dermatology* of 1905 Dr. Crocker described a disease which closely conformed to the case exhibited. He also stated that the name "xantho-erythrodermia perstans" was suggested by Dr. Pernet. The same condition was described, under the name of "parapsoriasis," by Brocq. It was a slightly scaly reddish-yellow, irregularly distributed collection of patches, mostly on the thighs, although there were a few lesions on the arms and trunk. Subjective sensations were so slight that the young man himself was not at all sure when he first noticed the eruption—he thought about a year ago. During the two months during which he had been treating him with various ointments and the Kromayer lamp, there had not been the slightest change either in number or appearance of the lesions. The eruption corresponded intimately to the seven points postulated by Brocq: (1) Almost complete absence of pruritus; (2) very slow evolution; (3) scattered, circumscribed, sharply defined patches of varying size (2 to 6 cm.), and situated mainly on the thighs and

trunk ; (4) a pinkish coloration ; (5) absence of infiltration ; (6) slight branny desquamation ; (7) pronounced resistance to treatment of all kinds.

Dr. S. E. Dore showed two cases of *neurofibromatosis*. These were two striking examples of extensive multiple tumours of the skin. One, that of a woman, aged 44 years, was a typical case of molluscum fibrosum. She had had the condition seven years. There were numerous soft flat and protuberant tumours scattered over the body, some with blue discoloration, and there were also some patches of pigmentation. The other patient, a woman, aged 40 years, had had multiple pigmented growths from birth ; she said they had increased in number, and some had increased in size. There was also a large raised pigmented warty area of skin in the sacral region. Many of the small prominent tumours were free from pigment, and he had classed both these cases under the generic term of neurofibromatosis, but several members who had seen the second case consider it to be one of pigmented moles.

Dr. S. E. Dore showed a case of *parakeratosis variegata* in a man, aged 40 years. This was a case of what he believed to be parakeratosis variegata. The patient had had the eruption for twelve years : it began with three small patches on the trunk, and there had been a gradual increase in the number and size of the patches. There was considerable itching, especially when the patient became hot and sweated. For many years this man had driven a steam engine, and it was possible that exposure to heat had aggravated the condition. There were large circular patches of dermatitis scattered over his body of a deep red or brown colour, some of them having a retiform or stippled appearance. The recent patches were covered with fine scales and somewhat resembled psoriasis.

A patient, suffering from this disease, whom the exhibitor showed in November, 1922, who was originally shown by Dr. Wells Patterson at the Newcastle meeting of the British Medical Association, and was subsequently under the care of Dr. Cranston Lowe in Edinburgh, developed an indurated mahogany-coloured scaly skin and had recently died at the London Hospital from leukæmia. He remembered the late Dr. Pringle asking whether anything was known as to the further history of these cases of parakeratosis variegata. The case he referred to changed completely, as regards his cutaneous condition, from parapsoriasis to a

generalised scaly pigmented erythrodermia, and it would appear that the latter was related to the leukæmia rather than the former.

Dr. H. MacCormac said that mycosis fungoides might be suggested as an alternative diagnosis. It could be put to the test in two ways: by microscopic examination, and by the result of the application of X-rays—if it were mycosis fungoides, one would expect a rapid clearing up after X-rays. The long duration did not exclude mycosis fungoides, as in some cases the premycotic stage had existed for years. He did not know whether the infiltrated character of the lesions allowed the condition to be included under the term "parapsoriasis." The considerable degree of itching was of importance in the diagnosis.

Dr. W. J. O'Donovan confirmed the statement of Dr. Dore that a patient who was considered to have parakeratosis variegata had died in London Hospital, and a post-mortem examination had been made. He was taken in as a case of bronze diabetes, but when his blood came to be examined the condition was found to be that of leukæmia. This man, however, had a spleen which weighed 5 lb.

Dr. Gardiner said that at first he had thought this was a case of mycosis fungoides in the premycotic stage. There were several areas on the back which were distinctly atrophied, and there was a marked thickening on the thigh. There was also itching, and he agreed that premycotic itching might exist for years before nodules appeared. In most of the cases of parakeratosis that he had seen the areas chiefly involved had been the forearms, and there had been definite linear markings; the appearance was different from that in this case.

Dr. F. Parkes Weber said that in this case an early leukæmic condition could be practically excluded as there was no obvious infiltration of the skin, but a blood-count should be made. He thought there was danger of misunderstanding regarding the case referred to by Dr. O'Donovan; he had recently seen that case in the London Hospital (May 30th), and it was then very unlike the present case of parakeratosis. Practically the whole skin was infiltrated, and the patient (a man aged 60) had a definite leukæmic change in the blood. He had heard that the case had been claimed to be one of lymphoblastic erythrodermia, and he told Dr. Robert Hutchison, who kindly allowed him to see the case, that if the liver could be examined it would probably be found to show lymphocytic (leukæmic) infiltration. Probably all the cases published by Dr. Sequeira and Dr. Panton as lymphoblastic erythrodermia were leukæmic skin cases of the class described by Kaposi under the term "lymphodermia perniciosa."

Dr. Graham Little said that he supported Dr. Dore's view. He did not think this was a case of mycosis fungoides, but one of parapsoriasis.

Dr. S. E. Dore showed a case of *extensive linear nævus* in a man, aged 54 years. This was an extensive linear nævus, and somewhat resembled the case of a girl which Dr. Stowers described many years ago. In this patient the nævus was on both sides of the face, but was on the right side of the body only. On the face there were masses of closely aggregated, deeply pigmented papillomatous lesions. There was a long streak in the central line of the abdomen, a large patch in the right groin, and another

streak extending down to the foot. Some of the growths were removed surgically from the chin, but they had to a certain extent recurred. He did not think it was worth while attempting anything in the way of active treatment.

Dr. J. H. Stowers said that this case corresponded in many particulars with the one he (Dr. Stowers) had shown before the Section some years ago, full details of which were published with illustrations. He agreed with Dr. Dore that surgical treatment alone was likely to be of service to the patient.

Dr. Henry MacCormac showed a case of *mycosis fungoides*. The patient, a male, aged 37 years, stated that about four years ago he noticed some small lumps on the right side of the left ankle. About two years later the local practitioner who first saw the condition, considering it to be syphilitic, sent the patient to hospital, where a diagnosis of mycosis fungoides was made. The disease by this time had spread considerably, the patient being extensively affected on the trunk and limbs. He was treated with X-rays, following which the eruption completely disappeared. Three subsequent relapses had occurred, the condition as seen at present being more extensive and severe than any of the others. It was formerly possible to remove the eruption with comparatively small doses of X-rays, but the lesions, especially the tumour formations which were represented here and there, were now much more resistant, requiring a full pastille dose. Repeated blood-counts had been made, but despite the very extensive application of X-rays to the skin surface no degree of anæmia had as yet become evident. There was a slight leucocytosis.

Dr. Henry MacCormac showed a case of *dermatitis artefacta*. The patient was a single woman, aged 24 years, by occupation a cook. Eleven months ago she burned both legs with hot fat, but whereas the lesions on the left leg healed rapidly, those on the right persisted. When the patient was seen at hospital (February, 1923) there was a large erythematous patch on the right leg, with superficial scar-formation, peculiarly translucent, and showing numerous superficial vessels just beneath the surface. The lower margin was marked by a well-developed erythematous border, which was slightly eroded. No progress was made while the patient remained an out-patient, but after admission to the ward and enclosing the affected part in plaster-of-Paris complete healing took place, the scar alone marking the site of the eruption.

Dr. H. W. Barber showed a case of *morphœa associated with vitiligo*. The patient, aged 54 years, male, dock labourer, had had pruritus scroti for about thirty years, and came to him in May of this year for this symptom. On examination, apart from lichenification of the scrotum, vitiligo of the penis and groins was observed, and a large area of morphœa with lilac border in the mid-line of the lower part of the back and symmetrical patches of morphœa on both sides of the lower abdomen and groins. As these patches did not attract the patient's notice he did not know how long they had been present. Physical examination revealed no abnormality except very severe oral sepsis. Wassermann reaction negative.

Mr. Bulleid had investigated the mouth. Apart from gingivitis, pyorrhœa with pockets, radiograms revealed extensive apical infection of the teeth with marked bony changes in the alveolus. Several teeth had been removed, and a pure growth of *Streptococcus longus* was recovered from the apices. This organism was agglutinated by the patient's serum in dilutions of 1 in 20 and 1 in 200.

Streptococci obtained from the tonsils were not agglutinated. Cultivations of the fæces (three specimens) gave only *Bacillus coli* and a few colonies of *Streptococcus fæcalis*, which was not agglutinated by the patient's serum. Since being in hospital the patches of morphœa had become much less evident.

On February 28th, 1908, Dr. Adamson showed a case of sclerodermia and leucodermia combined in a patient, a girl, aged 16 years. On the neck and chin on the left side there was a large irregular area of leucodermia with a margin of deeper pigmentation and some finger-nail-sized pigment macules over the white area. Occupying part of the same area were three elongated patches of sclerodermia. Apart from the interest of the unusual association of leucodermia and sclerodermia was the fact that the distribution corresponded very closely with the sensory area of the second and third posterior cervical roots. Towards the chin, however, it overlapped this area and passed on to that of the third division of the fifth cranial.

Dr. F. Parkes Weber regarded the present case as a genuine example of the association of vitiligo and the morphœa form of sclerodermia, but in some other cases the supposed vitiligo lesions were in reality only part of the sclerodermia.

Dr. A. M. H. Gray showed a case of *generalised sclerodermia with subcutaneous nodules*. The patient was a young woman, aged 26 years.

She had diffuse sclerodermia with a four years' history. It started as the hypertrophic œdematous form, which gradually subsided, and she now presented the typical atrophic form. It was apparently getting considerably better. The interest of the case lay in the fact that during the last year she had noticed numerous subcutaneous nodules. They were limited to certain parts of the body, and appeared to be attached to the tendon-sheaths, capsules of joints, and periosteum. On the tendon-sheaths at the backs of the hands were many of them, closely arranged in lines: their size was a little less than that of a lentil. There were many in the region of the hamstring muscles, and on the dorsum of the foot. In addition there were large fibrous nodules attached to the periosteum in the neighbourhood of joints and along the iliac crests. The largest nodules were on the back of the scapulæ or attached to the spinous processes of the dorsal and lumbar vertebræ. There were a few scattered about on either side of the spine, apparently not attached to periosteum nor to the deep fascia. He had removed two of them from the dorsal region, and they were not fixed down to the deep fascia, but were free in the subcutaneous tissue.

Subcutaneous nodules were not very uncommon in sclerodermia; and Crocker believed that they would be found to be common if they were looked for. But, apart from calcareous nodules, there had been very few references to nodules not of a calcareous nature. He had had some of the nodules in this case X-rayed, and they were not calcareous. He had also examined sections, and these did not show any deposit of chalk in the tissues. Microscopically the fibrous tissue of the nodules had apparently undergone hyaline degeneration, and in addition there was a very closely packed round-cell infiltration round the vessels at the periphery of the nodule itself.

Dr. F. Parkes Weber said these nodules reminded him of the "rheumatic nodules" sometimes seen in young adults; and Radcliffe-Crocker had referred to the occasional occurrence of "subcutaneous nodules of the rheumatic type" in association with sclerodermia. In the present case the distribution of the nodules about the scapulæ and iliac crests resembled that of rheumatic nodules. He (Dr. Weber) had seen the case in August, 1922, and had then specially noted the beaded (nodular) condition of the tendons or tendon-sheaths at the back of the hands.

Dr. W. Knowsley Sibley showed a case of *acne varioliformis*. The patient, an unmarried woman, aged 26 years, was sent to him for a skin

condition from which she had been suffering for over four years. The lesions were chiefly aggregated at the hair-margin of the forehead, but extended slightly down on the face in front of the ears. There were acneiform papules, leaving large well-marked scars. A group of similar lesions had been present on the upper dorsal region between the scapulæ, where some dozen very large varioliform-looking scars were present.

Dr. J. E. M. Wigley showed a *case for diagnosis*. This little girl was said to have had a recurrent blister eruption every year since she was vaccinated at 6 weeks of age; she was now aged 12 years. The blisters and pustules were situated chiefly on all four extremities, and there were a few on the trunk. The eruption appeared in the spring, remained during the summer, and disappeared in the winter. This year, for the first time, pustules had occurred: previously there had been only blisters. Itching was said not to have been very severe, but more marked at night. Cultures from the clear blisters were sterile, but from the pustules they obtained a long chain streptococcus in pure culture. The Wassermann reaction was negative. He thought it might be a case of dermatitis herpetiformis.

Dr. J. E. M. Wigley showed a case of *lichen spinulosus*. Patient, a child, aged 4½ years, apparently healthy, had a local condition which he thought was lichen spinulosus, associated with a mild degree of xerodermia, and he thought there was some evidence of early achondroplasia. There was marked lordosis and shortening of the upper portions of its limbs. The Wassermann reaction was negative.

Sir G. Archdall Reid described a *new method of treating skin diseases*. In treating the cases which would be shown, he had been using salicylic acid in great strength—50 per cent. by weight in vaseline and about 12 per cent. in collodium. His idea was that, when weak preparations of the acid were used neither the pathogenetic organisms not the surface tissues were destroyed; as a consequence, absorption, inflammation, and perhaps poisoning resulted; but, if the acid were used in great strength, the surface tissue and the contained organisms would quickly be killed, and the dead layer formed would protect against absorption. Apparently this was what happened. On healthy skin the layer of tissue destroyed by this treatment was no thicker than tissue paper. On diseased surfaces little besides the affected tissue perished. The whole thickness

of the epidermis was not destroyed, except perhaps in minute, punctiform, diseased areas. The 50 per cent. ointment might be left on for days, and in a day or two after its removal a smooth, unbroken skin was generally to be seen. He tried this ointment on himself first, and then, very cautiously, on patients. He had never had any ill-results. There had never been undue pain, or much inflammation, or so much as a suggestion of poisoning. Now he used it boldly over large areas.

The following notes briefly indicated the results of treatment in certain skin diseases :

Lupus.—In the treatment of lupus by this method swift improvement results—especially in the case of lupus vulgaris. The cosmetic results were excellent. But he had never yet achieved complete cure. Of two female patients shown, one would be seen with a scar on her nose. A fortnight ago she had an open sore and the nostril was being eroded. He had brought her to show that salicylic acid, used in strength, healed, but did not destroy. The other lady, whose condition had greatly improved, had extensive lupus erythematosus of many years' standing over one eyebrow and on a large area of scalp.

He had one case of scabies in which he treated the patient with the ointment, and recovery very rapidly followed.

Ringworm.—There were several cases for demonstration, two or three of which were only half cured, and he had brought the patients to show how little irritation was caused by the ointment, rubbed in for ten minutes twice a day. Dr. Victor Blake, who was in charge of the Portsmouth school clinic and who had tried the treatment, had also brought some cases of ringworm, and these he would describe himself.

Dermatitis.—But the most striking results were seen in cases of dermatitis, erythematous, vesicular, papular, scaly, acute, chronic, some very extensive. The results of the treatment were summarised in the following cases shown :

Case 1.—This was the case of a young girl, aged 16 years, who, a month ago, developed acute vesicular dermatitis on the side of her face and neck. Now they could see only faint traces of past trouble. Her fresh complexion indicated how little injury was caused by the strong ointment.

Case 2.—That of a young woman who two months ago suffered from very acute vesicular dermatitis over one side of her face and neck and over both arms and hands. In less than a week there was small trace of disease left. She suffered great pain on the first day of treatment, less

on the second, still less on the third, and on the fourth she was without pain. This was a common experience.

Case 3.—Patient, a man, was a baker. He had been under private treatment, and as he was getting no relief he was advised to attend the hospital. A month ago he came to him with his forearms a mass of scabs. In a few days he had greatly improved. But when he was about to return to work he suddenly developed acute dermatitis of both legs below the knees—so acute that the legs became œdematous. That was a fortnight ago; but beyond some redness and roughness of the skin he had little trace of the trouble now.

Case 4.—Patient, a female, who had a papular vegetative dermatitis of the arms and hands for fourteen years. In a week she had not a trace of it.

Case 5.—Patient, a female, had papular dermatitis of both forearms, and scaly dermatitis from the middle of her thighs to her ankles for eight years before she came to him about two months ago. She, too, now had hardly a trace of the trouble remaining. But unfortunately she showed great tendency to relapse when she discontinued the ointment.

Dr. Victor J. Blake said it was only within the last month or six weeks that he had tried the treatment, but in cases of acute dermatitis, eczema, etc., he had had one or two remarkable results. One was a child whom he had hoped to bring to the meeting; she was aged 6 years, and had had trouble since her second year. All kinds of treatment had been tried, but four days after commencing Sir Archdall Reid's treatment the condition was well, and that was a month ago. In two other cases the eczema healed in two or three days. When the surface was raw he felt some compunction about applying this strong treatment, but he did so, and in four days the condition had cleared up, and there had not been any recurrence. With regard to ringworm cases, he was somewhat of a sceptic. Having many ringworm cases to deal with, he had given up treating them by drugs, and had relied upon X-rays. However, since using the method now under discussion he had had several cases in which there was very rapid improvement. He was never satisfied with a case of ringworm unless he could find the scalp free from infected hairs, and the microscope showed no spores; but in the cases they had had submitted to this treatment there seemed microscopically to be a marked degeneration in the spores. A small child under his care was given the treatment a month ago, and its ringworm was now absolutely cured. Equal parts by weight of vaseline and salicylic acid were used, and the efficacy of the ointment thus compounded was very much greater than that of all the ointments which had been tried for ringworm.*

* Owing to the lateness of the hour no opportunity was given to members of the Section to discuss the cases shown.

CURRENT LITERATURE.

INFLAMMATIONS, ETC.

HERPES ZOSTER GENERALISATUS. Mihran B. Parounagian and Herman Goodman. (*Arch. of Derm. and Syph.*, 1923, vii, p. 439.)

A case is here reported of a man, aged 64 years, who presented a well-marked eruption of herpes zoster on the right abdomen, in addition to which there was a generalised eruption of scattered vesicles on the trunk, axillæ, thighs, shoulders and arms. The face and buccal mucosa were free from lesions. The diagnosis arrived at was generalised herpes zoster. The literature on this subject is reviewed, and the paper ends with a comment on the question.

The authors consider that there is a definite group of cases which is best identified as generalised herpes zoster, and that this is distinct from the fortuitous association of herpes zoster and varicella. They are inclined to support the contention, assuming that herpes zoster is due to changes in the posterior root ganglia in the spinal nerve, or in the ganglia connected with the sensory cranial nerve, that when the herpetic eruption is accompanied by much local disturbance of sensation, the inflammation has overflowed along the sensory roots into the grey substance of the posterior horns, and that this may conceivably be registered on the skin by a generalised eruption of vesicles.

J. M. H. M.

BRACHIAL HERPES ZOSTER AND VARICELLA. De Vaugiraud. (*Journ. des Sciences Medicales de Lille*, 1923, xli, p. 229.)

A case of herpes zoster is reported in a child, aged 5 years, with extensive distribution over arm, forearm and hand. Two sisters developed varicella sixteen days after the first appearance of the zona. A review of the literature is given on the question of the possible interdependence of varicella and herpes zoster.

M. G. H.

THE TREATMENT OF PRURITUS ANI WITH BACTERIAL INJECTIONS. Frank Crozer Knowles and Edward F. Corson. (*Arch. of Derm. and Syph.*, 1923, vii, p. 505.)

According to the observations of the writers, injections of *Streptococcus fæcalis* vaccine offer the best means of curing pruritus ani. The dosage should be large and continued over a considerable period. All pathological conditions should be excluded before this method of treatment is adopted.

J. M. H. M.

PRURITUS ANI. Y. F. Montague. (*New York Med. Journ.*, April 18th, 1923, p. 469.)

The author divides pruritus ani into (1) direct pruritus and (2) indirect pruritus. Under direct pruritus he groups those cases in which trauma of the peripheral nerve-endings occurs by virtue of abrasions, avulsion, compression, physical or chemical maceration of the epidermis and its nerve-endings.

The cause of indirect pruritus he ascribes to chronic dyspepsias of all kinds, carcinoma of the stomach, chronic colitis, chronic constipation and fæcal

retention. Chronic endometritis, prostatitis and urethritis, as well as hypertrophic cirrhosis of the liver, chronic nephritis and cholecystitis are also alleged to be the cause in certain cases. The author puts forward the hypothesis that any alteration in size of a viscus stimulates the posterior spinal ganglion, and is thence referred to the skin of the area supplied by the particular somatic afferent nerve affected. W. F. C.

DISEASES OF ECTODERMAL ORIGIN: (1) MENTAL DISEASES AND HEREDITARY CUTANEOUS ANOMALIES, ESPECIALLY ICHTHYOSIS; (2) CHANGES IN THE PERIPHERAL NERVES OCCURRING IN ICHTHYOSIS AND v. RECKLINGHAUSEN'S DISEASE. J. Henrichs and P. Henricksen. (*Norsk Mag. f. Lægev.*, January, 1923, p. 1.)

The first part of this very interesting communication is the continuation of a previous article by Henrichs, of which an abstract appeared in the *British Journal of Dermatology*, xxxiii, p. 125.

The case of an imbecile is reported with an ichthyotic skin condition and other lesions suggesting (clinically) those of Darier's disease, particularly the involvement of the nails. The histological appearance is recorded, and mention is made of the microscopical changes of the skin described by Boeck in the condition ichthyosis sebacea. To further elaborate the theory of an ectodermal aplasia to explain the common origin of ichthyosis occurring with mental disease, attention is drawn to other conditions, viz.: colour-blindness and dysleksia associated with ichthyosis, juvenile cataract and adenoma sebaceum with sclerosis tuberosa cerebri (though this condition is not so definitely hereditary), v. Recklinghausen's disease with psychical changes.

In the second paper Henricksen describes the microscopical changes found in nerves from cases of (1) ichthyotic imbecile, (2) v. Recklinghausen's disease. In both cases there was an extensive degeneration coupled with new formation of nerve-fibres. In ichthyosis the nuclei of the neurilemma, while not numerous were deeply stained: in v. Recklinghausen's disease the neurilemma cells showed lively proliferation without any marked "activity" staining reaction, the whole appearance resembling that to be found in the central stump, after a nerve cutting, when the myelin is beginning to appear.

Finally there is an English summary of both papers. W. J. O.

DIFFERENT FORMS OF LEPROSY, ESPECIALLY LEPRA TUBERCULOIDES. H. P. Lie. (*Medicinsk Revue*, January–February, 1923, p. 143.)

The tuberculoid form is a distinct type of leprosy, the association of any nerve affection pointing to this diagnosis, while the skin lesions resemble more closely those of tuberculosis. The histological appearance with giant-cells of the Langhans type makes the differential diagnosis no easier. *B. lepræ* have been found in these tubercles before the occurrence of central necrosis. This is analogous to their presence in the early macules, or in the spreading edge of the same when absent in the pale centre. The clinical behaviour of these particular lesions is different to that of the ordinary leprous nodules, and with their more rapid disappearance suggests the expression of a peculiar protective skin reaction.

W. J. O.

TREATMENT OF NODULAR LEPROSY WITH CO_2 SNOW.

Prof. A. Paldrock. (*Arch. f. Derm. u. Syph.*, cxliii, sect. 1–2, p. 21.)

On September 20th, 1922, the author demonstrated a female patient, who, after thirteen months' treatment by local freezing, had lost all external manifestations of the disease. Two other successful cases were cited.

Paldrock explains that in his view the cause of therapeutic failure up till now is the existence of an albuminous capsule which protects Hansen's bacillus from the approach of defensive antibodies. This capsule is destroyed by the virulence of the local reaction, and the unchained bacillary stimulus (antigen) then evokes the specific antibody. That this is the probable explanation is supported by the interesting and important fact that treatment of a single group of nodules apparently caused the spontaneous involution of others to which the CO_2 pencil had not been applied.

The fragmentation and disappearance of intra-nasal bacilli *pari passu* with the treatment of the cutaneous nodules would seem to offer further evidence of the efficacy of the method, which, as above stated, is thought to be due to the unmasking of antigen and a resulting mobilisation of specific antibody.

[Details of duration and frequency of applications of the snow are not here divulged.—*Trans.*] H. C. S.

SERUM REACTION FOLLOWING SUBCUTANEOUS INJECTIONS OF HÉMOSTYL.

G. Didier. (*Journ. des Sciences Medicales de Lille*, 1923, xli, p. 221.)

A girl, aged 22 years, who had not previously received an injection of serum, suffered from urticaria, headache and anorexia following injections of hémostyl given for hæmorrhage after operation for deviated septum The suggestion is made that sensitisation was due to eating horse-flesh, which the patient was in the habit of doing once or twice a week. M. G. H.

CHEILITIS EXFOLIATIVA AND ITS TREATMENT WITH X-RAYS.

Robert Abimelech. (*Ann. Derm. et Syph.*, 1923, vi serie, iv, No. 2, p. 85.)

The author refers to two cases of cheilitis exfoliativa, both apparently cured with X-rays. The first patient, an unmarried woman, aged 37 years, had had the condition for six months, and treatment with various ointments had failed. There was no acne or seborrhœa. She was given applications of X-rays—four hours with a 1 mm. filter of aluminium over a period of six days. The actual dosage is not stated. The desquamation of the lips ceased at the end of a week, but recurred three weeks later. Another series of applications of the rays without a filter brought about a cure. The second patient had seborrhœic lesions on the scalp and face. Two series of applications of the rays of four hours each resulted in cure. H. W. B.

A SUGGESTED ÆTIOLOGY OF BAKERS' DERMATITIS.

De Jong. (*Lancet*, May 5th, 1923, p. 894.)

The author has investigated the various older theories as to the causation of this affection, *i. e.* parasites in the flour, sensitisation to flour proteid, chemical "improvers" and yeast or other fungi.

Inquiries at flour mills showed that although workers there may be covered with flour-dust day after day, cases of skin trouble on the arms are practically unknown.

The flour from bakehouses where patients were suffering from dermatitis was examined and no chemicals, acari or fungi were found to be present.

Inquiries found at the distillery revealed no instances of dermatitis in the men engaged in dealing with the yeast.

The author attributes the dermatitis to the 3·6 per cent. solution of salt in which the arms of the worker are frequently immersed, and notes the important point that the worker has often to leave this mixture to attend to the ovens, when the salt crystallises on the arms and hands, these crystals being worked into the skin by the subsequent process of kneading.

Dermatitis due to salt is found in workers other than bakers, *i.e.* herring salters and packers and rock-salt workers.

A preliminary note as to prophylaxis is the suggestion that a "rose spray" of running water be provided, under which the arms should be rinsed at frequent intervals. J. A. D.

INDUSTRIAL HYGIENE: EXPERIMENTS WITH OILS. J. E. Heestermann. (*Münch. med. Wchnschr.*, December 22nd, 1922, p. 1771. Reviewed as follows in *Journ. Ind. Hygiene*, May, 1923, p. 11.)

Heestermann, experimenting with a view to determining the exact cause of the different skin lesions caused by machine oils, used various lubricating and cutting oils, rubbing them on the shaven skins of rabbits, and found that the irritating substances belong to the more volatile constituents of the oil; but that they are neither of basic nor of acid nature, nor do they belong—as Weichardt and Apitzsch thought—to the unsaturated compounds, nor are they asphalts. They can be removed from the oils by purification with sodium hydrate and sulphuric acid. R. P. W.

CERTAIN DERMATOSES OF MONKEYS AND AN APE. Fred. D. Weidman. (*Arch. of Derm. and Syph.*, 1923, vii, p. 289.)

The observations included in this paper were made at the Laboratory of Comparative Pathology of the Philadelphia Zoological Gardens. The diseases referred to consist of pemphigus, scabies, sebaceous cyst, subcutaneous œdema, blastomycetic dermatosis, and tinea capitis et circinata.

An attack of scabies was described in an orang-utan, in which the mite had the same morphology as that of the human, and in which the diseases was transmitted to the orang-utan's keeper. The blastomycetic dermatosis occurred in the axillæ of a monkey, which was sacrificed at the Zoological Gardens as a tuberculosis suspect. There was a scaly condition of the axillæ, and from this a yeast was recovered. J. M. H. M.

GRANULOMA INGUINALE. I. M. Gage. (*Arch. of Derm. and Syph.*, 1923, vii, p. 303.)

This condition occurs in the United States, being endemic in some of the extreme Southern States. In this paper four cases are described.

The writer considers that the cause is an organism, described by Donovon, which is believed to be a protozoan. This organism either occurs in the cytoplasm of an endothelial leucocyte, or free from the cells. The organisms are usually situated near the nucleus of the cells, unless when they are in abundance, when they practically occupy the entire cytoplasm. They vary in form, some being like cocci, others bipolar, or in the form of short rods.

Clinically the picture is familiar, and consists of a sclerosing granuloma. Tartar emetic, administered intravenously, seems to be a specific, but when the lesions are accessible to surgical excision, this procedure should be combined with the injections. J. M. H. M.

GRANULOMA INGUINALE (ULCERATING GRANULOMA). H. Goodman. (*Urol. and Cut. Review*, February, 1923.)

This short article gives a pictorial presentation of the various clinical appearances of ulcerating granuloma and the conditions which simulate it.

There are thirty photographs, including some showing the histological changes, which show no specific features, and photographs of organisms of Calimatobacterium (granulomatis type), and another organism claimed to be the cause—*Spirochæta aborigiualis.*

Two cases are recorded in married women, whose husbands were unaffected. Successful treatment with intravenous injections of tartar emetic is recorded.

W. H. B.

STRIÆ CUTIS DISTENSÆ IN SHIGA-KRUSE BACILLARY DYSENTERY. Brünauer. (*Arch. f. Derm. u. Syph.*, cxliii, sect. 1–2, p. 110.)

Based on the histological appearances of the skin in two cases, the author believes that the direct cause of the damage to the elastin was a specific toxin. The theory of mechanical distension could not be applied, as there was none at any time during the illness; and the development of the condition in these two cases, in which it was carefully watched throughout, strongly supports the theory of Aschoff that elasto-toxic material circulates in the blood of infectious cases.

H. C. S.

GONORRHŒAL KERATOSIS. S. L. Bogrow. (*Arch. f. Derm. u. Syph.*, cxliii, sect. 1–2, p. 23.)

A short summary of this long thesis would seem to emphasise the following points:

(1) The so-called gonorrhœal keratoses belong to the inflammatory exudative group, and the parakeratotic manifestations so highly characteristic of the condition are of secondary origin.

The mucous membrane of the mouth (as in the particular case reported) can be affected as a very rare complication.

(2) The development of the keratoses can occur both in the acute and chronic types of specific urethritis, and even when the gonococcus has disappeared from the genito-urinary tract, but then only in cases in which there are symptoms of general infection.

(3) The infections are probably metastatic in type.

(4) Cases without gonococci in the urethra, etc., run an atypical course, and resemble then the arthritic types of psoriasis.

(5) Treatment results are best when vaccines are combined with local treatment of the urethra and the joints. H. C. S.

WATERLOGGING IN PEMPHIGUS VEGETANS. Kartamischew. (*Arch. f. Derm. u. Syph.*, cxliii, sect. 1–2, p. 184.)

As a result of observations on a moderately severe case of this disease in a patient of 67, which began on the tongue, and spread thence to neck and axillæ, the author believes himself justified in the following conclusions : (1) A tendency to water-retention and increased absorption occurs in pemphigus. (Explanation was not forthcoming.) (2) During acute eruption there is NaCl retention, and the excretion returns gradually to normal as the outbreak subsides. A similar curve for eosinophilia can be demonstrated *pari passu* with the above. (3) These curves are strictly comparable with that which occurs in the Wassermann reaction as a case of lues improves. H. C. S.

HERPES GESTATIONIS. O. Bittmann. (*Českú Dermatologie*, 1922, iv, p. 33.)

A patient in the third month of her fifth pregnancy developed an extensive herpes gestationis accompanied by severe dyspeptic symptoms and stubborn constipation. Working on the theory that the cells of chorionic epithelium produce active ferments with a specific function and that their disintegration forms in the organism of the pregnant woman antiferments paralysing their function, the author considered the case in question as one of disturbed balance in the production of ferments and antiferments. To supply the missing maternal antiferments he injected five doses of 10 c.c. each of normal pregnant serum. The eruption as well as the dyspeptic symptoms disappeared. After a week's interval a recurrence took place which again cleared up after two doses of serum. The third recurrence sixteen days later was very severe and resisted further doses. Two doses of 14 c.c. of boiled milk, followed by a severe reaction, cleared up the skin lesions permanently, the non-specific protein therapy proving much more efficient than the specific serum. The therapeutic effect was undoubtedly one of activation of the protoplasm in a pathological organism.

Spinka (St. Louis).

CONCERNING PATHOGENESIS OF EPIDERMOLYSIS BULLOSA HÆMORRHAGICA. Ladislav-Kucera. (*Českú Dermatologie*, 1922, iv, p. 65.)

After extensive studies of the blood of a previously reported case of epidermolysis bullosa hæmorrhagica the author arrives at the following conclusions : (1) Epidermolysis bullosa hæmorrhagica bears no relation to the group of the so-called hæmorrhagic diatheses. (2) The composition of plasma, blood functions and the capillaries show no deviation from normal. (3) The morphological blood picture shows an absolute and a relative lymphocytosis of a moderate degree ; neutrophiles and monocytes show a parallel decrease.

Spinka (St. Louis).

REVIEW.

Diseases of the Skin.*

Dr. MacKenna has written a book, primarily intended for students and practitioners, which is a credit to British dermatology. His exposition is exceedingly clear and sufficiently didactic to enable those not well versed in the intricacies of dermatology to grasp with ease the essentials of the subject. Further than this he has, by the use of smaller type, included most of the less common, and therefore, from the standpoint of the practitioner, less important diseases. This latter feature has enabled the author to give a very complete survey of the whole field of dermatology. The book is imposing in its make-up and is of quite moderate proportions: its illustrations—all in black and white—are not only selected with judgment but are exceedingly well reproduced. The author is essentially practical in his methods of treatment, and this feature will prove a boon to the busy practitioner.

Dr. MacKenna is in the same difficulty as regards classification as are all who have tried to write a text-book on dermatology. He has chosen, as far as possible, an ætiological classification—the method now adopted in most recent English text-books. It may be questioned, however, whether a strictly ætiological classification is the best for teaching purposes; for example, it might be considered advisable for the student to realise the character of reactions of the skin to simple chemical and physical agents before he has to deal with the more complex reactions produced by micro-organisms. Further, it is of advantage to know something of certain abnormal conditions of the skin which predispose to inflammatory reactions, such as ichthyosis, before dealing with the inflammations themselves.

The author classifies granuloma annulare, the sarcoids and lupus pernio as tuberculides, though what little evidence there is as to the nature of these conditions is rather against their tuberculous ætiology. The statement that the acarus of scabies does not of itself produce any inflammatory reaction can hardly be borne out by experience, for burrows on the penis, in the gluteal cleft and on the anterior axillary fold are almost invariably accompanied by an inflammatory zone, while those on the hands are frequently associated with a vesicle, itself a manifestation of an inflammatory reaction. The diagram in Fig. 68 is also a little misleading as it shows no burrows in the genital area—a very common site—while it indicates burrows all over the back of the buttocks—a site in which they are very rarely seen if the adjacent parts of the gluteal cleft are excluded. Burrows on the feet are also not indicated but are not very rare.

The chapter on focal infection and sensitisation to foreign proteins is singularly lucid and complete, embodying all the most recent work on the subject. But this may be said for the book generally, and in spite of the small points mentioned the work is a notable addition to the dermatological library.

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* *Diseases of the Skin: A Manual for Students and Practitioners.* By Robert W. MacKenna, M.A., M.D., B.Ch., Hon. Dermatologist, Royal Infirmary, Liverpool. Pp. 451. 166 illustrations. London: Ballière, Tindall & Cox, 1923. Price 21s. net.

THE BRITISH JOURNAL

OF

DERMATOLOGY AND SYPHILIS

NOVEMBER, 1923.

ON THE FORDYCE-FOX SYNDROME.*

ARTHUR WHITFIELD, M.D., F.R.C.P.

This disease was described in 1902 by Fordyce in regard to the histological aspect and by Fox as to the clinical features.

The authors then described two cases, one a Russian woman, aged 28 years, and the second a young man, age not stated.

The salient feature of the cases was the presence of pinhead-sized, circular, domed papules affecting the hairy regions of the axilla and pubes, and associated with intense itching.

The histological features were briefly :

(1) Hyperkeratosis of the sweat-pores and hair-follicles, chiefly of the former.

(2) Consecutive acanthosis.

(3) Mechanical dilatation of the sweat-glands.

(4) Chronic inflammation of the derma.

Since this original communication the following cases have been reported.

In 1909 Fordyce reported a third case, female Austrian, aged 48 years, duration 1½ years. He then pointed out the benefit derived from sea bathing, and considered that the disease was a neuro-dermatitis probably of toxic origin.

Haase in 1911 reported a case in a female, aged 21 years, and described brittleness of the hairs which had dropped off, and also vacuolation of the prickle-cells. From his photographs I should be inclined to think that the vacuolation and the other slight differences from the Fordyce cases

* Read at the Third Annual Meeting of the British Association of Dermatology and Syphilis in Liverpool, July, 1923.

were due to scratching, since they closely resembled the condition seen in Hebra's prurigo.

Rasch and Kissmayer published cases in the *Dermatologische Zeitschrift*, and Brocq refers to it in his *Precis-Atlas*, 1921, grouping it under "Prurit circonscrit avec Lichenification."

Burnier and Marcel Bloch showed a case, Polish Jewess, aged 21 years, at the Société Française de Dermatologie in 1920. In this case the Wassermann reaction was examined and found to be negative. It is also noteworthy that in the discussion Darier remarked that the lesions did not resemble those of the Lichen simplex of Vidal.

Withers, in 1920, reported four more cases, all in females, aged respectively 13, 30, 32 and 45, and carried out numerous examinations with negative result, except that in one case the hæmoglobin was only 75 per cent. of normal and the red blood-corpuscles were 3,960,000.

Wallace Beatty, in 1921, reported two cases, females, aged respectively 22 and 23 years, all the symptoms and the histology being exactly like those described by Fordyce and Fox.

Walter, in 1922, reported a case in a female, aged 15 years, duration 6 months. There was considerable brown pigmentation of the affected areas and the hair was largely lost. The tuberculin and Wassermann reactions were both negative; the histology showed acanthosis without parakeratosis, but there were large, irregular pale cells at both the sweat-glands and the hair-follicles.

Barber, in 1922, showed a case in a young woman, age not stated, duration 2 years. In the discussion Pernet said he had seen cases with no clinical lesions but only the pruritus. In my opinion such cases cannot be legitimately included in this category.

Adamson referred to one case of his and pointed out the close similarity of the lesion to the plane wart.

Barber's case showed the characteristic histological features of the disease, and he suggested that they were due to chemically altered and irritating sweat. All observers seemed to be in agreement as to the failure of X-rays to cure the condition.

In March, 1923, Dr. Young, of Norbury, sent me the patient who is the reason for this communication.

The patient is a married lady, aged 37 years. Her past history shows that she had a complete nervous breakdown in 1914, was ill for some months, and since then has been intensely neurotic.

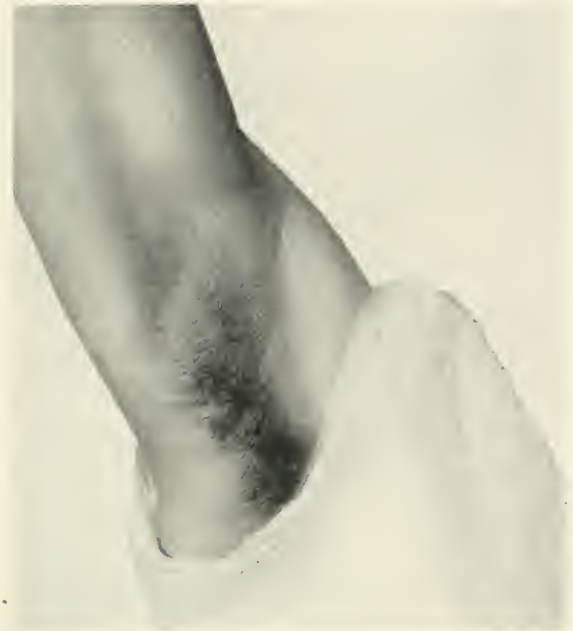

Fig. 1.—Right axilla, showing the characteristic wart-like papules.

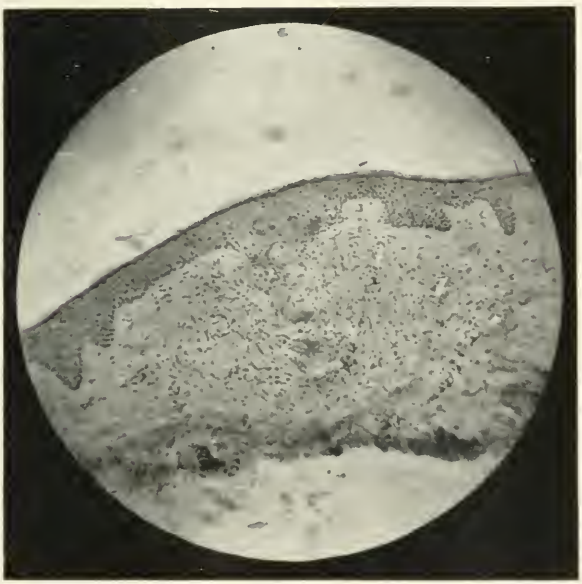

Fig. 2.—Section through centre of papule, showing contorted and acanthotic sweat-duct.

TO ILLUSTRATE DR. WHITFIELD'S ARTICLE ON THE FORDYCE-FOX SYNDROME.

About two years ago she began to suffer from intense itching of the axillary and pubic regions, and this has got steadily worse.

At the date of her first consultation her physical condition was as follows :

A tall and very slender woman with noticeably feebly developed musculature of the arms and legs, so that unless one saw the trunk one would believe her to be much thinner than she really is. The body is fairly well nourished, but there is some enteroptosis on standing. The face is somewhat sallow and the features drawn, probably owing to sleeplessness resulting from the itching.

Digestion on the whole poor ; flatulence and pain not severe, constipation absent ; passes mucus sometimes and has had colitis.

Gums very puffy and bleed readily on cleaning her teeth ; incisor teeth loose, many teeth already lost.

The axillary and to a less extent the pubic regions, the skin close around the umbilicus and the areolæ mammarum are affected by an eruption which is perfectly uniform in all its sites.

The only lesion evident is a circular papule, slightly less than one-sixteenth of an inch in diameter, of the colour of the normal skin, and arising from it abruptly to form an even, dome-shaped elevation. Where distributed most thickly the papules almost touch one another at their margins, but nowhere is there actual coalescence.

At first sight the papules appear to be follicular in origin, but closer examination with a lens shows that the hairs piercing them are in almost every instance slightly eccentric and that the real centre is the sweat-pore. This observation is further borne out by the occurrence of similar papules in the areolæ mammarum and umbilical region, where no hairs can be seen. There appear to be no different stages of development beyond very slight variation in size and prominence, and Adamson's statement that they resemble plane warts is certainly correct.

The patient was referred to her dental surgeon, who found the remaining teeth heavily infected and removed them. A catheter specimen of urine was obtained and found to be sterile on cultivation and no abnormal constituents were detected.

A sample of fæces was examined bacteriologically and was found to consist almost entirely of ordinary coliform organisms, a few enterococci only being found, and no lactose non-fermenters. The blood-pressure was examined and the systolic pressure was found to be 105 mm. Hg.

only; the diastolic pressure, which was not easy to define accurately, was found to be between 55 and 60.

Histology.—A papule lying a little outside the main aggregation in the axilla was excised and examined microscopically by serial section. It was found that there was little or no hyperkeratosis present, but there was marked acanthosis, forming in fact a small succulent warty growth, extending both upwards above the level of and downwards into the true skin. Serial sections showed that this was formed around the intra-epidermic portion of the sweat-canal as a centre, the canal being more acutely curved than is normal. Below in the true skin there was a hemispherical fibroblastic infiltration with formation of new collagenous tissue—apparently an attempt to circumscribe the downgrowth of the epithelium. I therefore think that the dilatation and degeneration of the sweat-glands described by others may be attributed to the epithelial overgrowth above and the constricting fibroblastic formation.

Pathology.—I may draw attention in support of the theory that I am about to put forward, first to the statement of Adamson that the little papules resemble plane warts, which is undoubtedly true clinically, and, except for the fact that much of the new growth takes place downwards into the true skin, is also true microscopically.

Secondly, I would draw attention to the curious and very limited distribution of the eruption, and I should like to point out that there are points of resemblance, with notable exceptions, to that found in acanthosis nigricans, and I would also draw attention to the fact that in some cases pigmentation has been noted though it was not obvious in my case.

Thirdly, I would allude again to the general lack of muscular tone, especially affecting the abdomen, and to the unusually low systolic blood-pressure—105 mm. Hg.

Now acanthosis nigricans is generally associated with malignant disease in the abdomen, and is, I believe, supposed to be due to some obscure involvement of the suprarenal-sympathetic system.

In the Fordyce-Fox syndrome we have a somewhat similar distribution of a somewhat similar lesion, though I do not wish to belittle the marked differences. If, however, we could be justified in assuming a very mild case of this disorder we should have a very similar picture, though I do not remember a case of acanthosis nigricans in which itching was a marked feature.

In addition to the clinical and histological features which may be taken

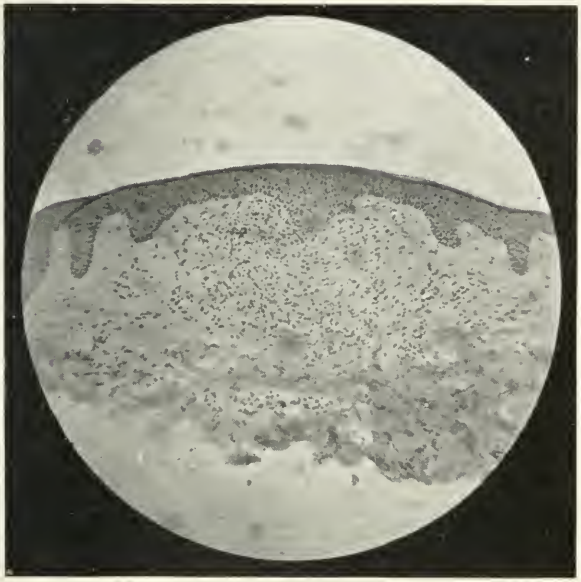

FIG. 3.—Section at edge of papule, showing lenticular fibroblastic infiltration.

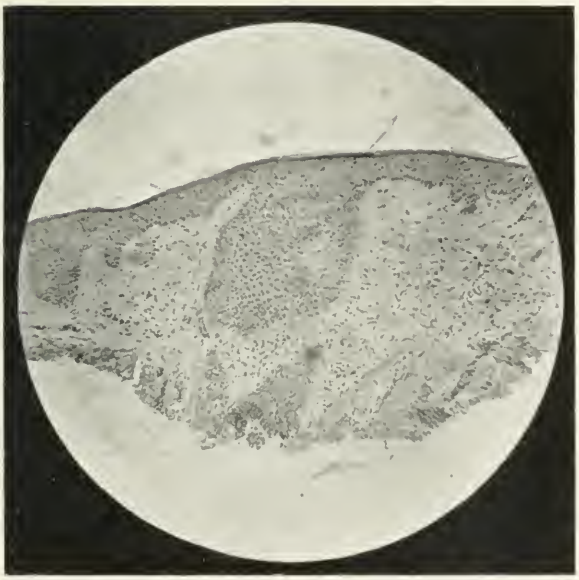

FIG. 4.—Section immediately beside sweat-duct, showing buried acanthosis.

TO ILLUSTRATE DR. WHITFIELD'S ARTICLE ON THE FORDYCE-FOX SYNDROME.

to show disorder of the suprarenal-sympathetic system we have the neurasthenia, present in all recorded cases, the loss of muscular tone, and the abnormally low blood-pressure.

My suggestion therefore is that the Fordyce-Fox syndrome is dependent on a suprarenal exhaustion.

Assuming this to be the case treatment would be naturally unsatisfactory, since suprarenal extract administered by the mouth is of doubtful value. I am, however, keeping my patient on pluriglandular extract for a time and watching its effect.

As regards symptomatic treatment, the great point is to relieve the intolerable itching. This I have succeeded in doing sufficiently to make life, according to the patient's statement, "again worth living," by the application night and morning of the following:

Phenol cryst.	ʒj
Camphor	ʒj
Acid. salicyl.	gr. xxv
Hydrarg. perchlor.	gr. ij
Glycerini	ʒj
Sp. vini methylat. (60 per cent.) .	ad ℥viij

In putting forward this endocrine theory I should like to insist that I am in agreement with Barber, who states that we ought always to try to get at the factor that is upsetting the endocrine balance, and it is for this reason that the obviously infected tooth sockets, the only organic error detected, were drained by removal of the teeth.

Finally I should like to pay a tribute to my old teacher, the late Dr. Colcott Fox, who, on abstracting Fordyce's second paper, had the clinical acumen to recognise the fact that the disease therein described was not ordinary lichenification. Haase in his paper pours some contempt on this observation, but it is substantiated by Darier, and I should like to register my opinion that in 1902 Fordyce and Fox described an entirely independent and well-defined clinical entity which is quite distinct from the lichenification produced by mere friction of itching skin.

Far from detracting from the value of their observation, this view seems to me to add to their merit in describing so accurately a disease which was completely unrecognised up to that time.

If it is not unfair to name a disease first described by others, I suggest the name acanthosis circumporalis pruriens.

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ON THE CONTRACTILITY AND NERVOUS SUPPLY OF THE CAPILLARIES.*

S. E. DORE, M.D.

Within recent years much light has been thrown upon two main factors which are fundamentally concerned in the production of cutaneous reactions.

These are the contractility of the cutaneous capillaries and the control of the capillary circulation by the nervous system.

The Contractility of the Capillaries.

A patch of erythema of the skin, whether produced by heat or cold, or by pressure with a blunt instrument or by nervous or toxic influences, is essentially a local hyperæmia caused by dilatation of the capillaries and an increased flow of blood through them. Speaking generally, anæmia of the skin is not an important productive factor of cutaneous disease. Until a few years ago the capillaries were regarded as elastic tubes undergoing passive distension in accordance with the general blood-pressure, the state of contraction or dilatation of the supplying arterioles and the nutrition of the vascular walls. There is now, however, con-

* Read at the Third Annual Meeting of the British Association of Dermatology and Syphilology in Liverpool, July 10th, 1923.

clusive evidence that the capillaries play an independent part in the peripheral circulation, that they possess the intrinsic property of contraction and relaxation, and are under the direct influence of the nervous system. This evidence, which rests chiefly upon the work of Dale and Bayliss in this country, and Krogh and his co-workers abroad, cannot fail to modify our conception of cutaneous reactions, and will, in some measure, help to explain their pattern and distribution.

(A full account of this new work on the capillaries will be found in the Oliver-Sharpey Lectures given at the Royal College of Physicians by Dr. Dale, and recently published in the *British Medical Journal* (1), the Silliman Lectures on "The Anatomy and Physiology of Capillaries" by Krogh (2), and the monograph of Sir William Bayliss on *The Vasomotor System* (3), and it is to these publications that I am chiefly indebted for the facts.)

It will only be possible to refer to some of the more important points, which for purposes of simplification I have tried to group under various headings, although it will be obvious that there must be considerable overlapping of the groups.

Microscopical.—There is now definite evidence that the walls of the capillaries, like those of the arterioles, are able to contract. The presence of contractile cells overlying the capillary endothelium was originally demonstrated by Rouget (4) in 1873, although Stricker (5) in 1860 described changes occurring independently of the blood-pressure in the capillary lumen in the nictitating membrane of the frog, and similar phenomena were described by Roy and Graham Brown (6) and other observers, but were attributed to changes in the capillary wall as a whole. Rouget's observations were confirmed by Mayer (7) in 1902, who also described intermediate forms between the Rouget cells and plain muscle fibres. In 1903 Steinach and Kahn (8), to whose claim to have discovered contractile cells in the walls of the capillaries I referred in a paper published in 1906, showed not only that the capillaries contracted as the result of stimulation, but that, like the arterioles, they were supplied by nerves from the sympathetic system. The presence of contractile cells in the capillaries has been recently corroborated by Vimtrup (9), working in Krogh's laboratory. This observer demonstrated the presence of flat branching cells on the outer side of the epithelial wall, encircling it with fine processes, contraction beginning at one or more of these cells, which appear to be continuous with the muscle coats of the arterioles and venules,

transition forms, as described by Mayer, occurring between plain muscle fibres and the Rouget cells.

Physiological.—Physiologically cyanosis of the skin produced by cold is evidence of capillary dilatation; the blue colour of the blood in the capillaries is due to loss of oxygen, indicating a slow flow of blood through widened capillaries, and this, as Bayliss points out, can only be explained by a dilatation of the capillaries in conjunction with constriction of the arterioles.

Chemical.—Various chemical substances produced either as the result of normal cell metabolism or of pathological changes in the tissues are known to cause dilatation of arterioles and probably also of capillaries. Carbon dioxide, which Starling ([10]) describes as the universal hormone set free in the circulation when the activity of the body as a whole is increased, causes local vaso-dilatation by its effects on the walls of the vessels. Severini ([11]) showed by experiments on the excised mesentery that carbonic acid dilated and oxygen constricted the capillaries. Dale and Richards ([12]) found that small doses of adrenalin caused a fall of blood-pressure, and that this was due to capillary dilatation. Further evidence of capillary dilatation was supplied by Dale and Laidlaw ([13]) from their observations on the action of histamine. Histamine, like adrenalin, when given in small doses is a capillary dilator, but these observers failed to obtain the dilator effect in the perfused organ, until they added red corpuscles and a small quantity of adrenalin to the perfusion fluid, showing that capillary tone was essential for the depressor effect to be manifested. There appears, however, to be no evidence that histamine is produced under normal circumstances, and Bayliss regards the quantity of adrenalin liberated in the circulation as insufficient for the maintenance of capillary tone. Another hormone, pituitrin, is a possible factor in controlling capillary tone. According to Pohle ([14]), removal of the pituitary gland in frogs is followed by cutaneous œdema and by contraction of the pigment-cells of the skin, which becomes much lighter in colour. Krogh, however, in repeating the experiments of Pohle, did not observe the œdema, and in perfusion experiments found that if pituitary extract is to be accepted as containing a hormone normally present in the blood, it must be shown to be active in much smaller concentrations. A diffusible substance has been found in mammalian blood-serum which possesses the property of maintaining capillary tone, and which resembles pituitary extract in many of its reactions, but

although Dale considers that the identity of this substance with pituitrin is not established, he is of opinion that the action of the suprarenal and pituitary glands exercises an important influence on normal capillary tone.

Some important observations made by Burn ([15]) and quoted by Dale may be mentioned here to illustrate the difficulty of distinguishing nervous from chemical effects. After section of the sympathetic fibres to a cat's foot, he found that the sweating produced by pilocarpine and the vaso-dilator response to histamine could still be obtained. When the mixed nerve to the limb was divided the response to pilocarpine and histamine disappeared, although the arterial dilator effect of acetyl-choline remained unaltered.

The pilocarpine and histamine response could, however, be restored by injections of adrenalin, and the impaired vitality of the skin of the foot, as shown by loss of hair, œdema of the skin, loss of flexibility, and a tendency to ulceration on exposure to pressure from walking, was also restored by adrenalin injections.

Experimental.—Experimental evidence of independent capillary contraction was provided by Cotton, Slade and Lewis in their paper on "Dermatographism, with Special Reference to the Contractile Power of Capillaries," published in 1917.([16]) These observers found that the red and white *tâche* and the pallor following an injection of adrenalin could still be produced after obstruction of the arterial circulation in a limb.

Krogh showed that single capillaries in a frog's tongue dilated as the result of local stimulation with a fine glass needle, and that the distance that the dilatation spread depended upon the strength of the stimulus.

Pathological.—The similarity between the action of histamine and the products of protein cleavage which cause anaphylactic shock led Dale and Laidlaw to suspect that the effect of these substances was exerted on the capillaries. Vaughan ([17]) showed that the heating of protein with alkalis in alcohol produced an intensely toxic product, and commercial peptones, when heated with acid or alkaline alcohol, give rise to a highly toxic substance, having all the properties of Vaughan's soluble protein poison, called by Popielski "vaso-dilatin." Clark ([18]), however, found that histamine, unlike vaso-dilatin, was practically non-toxic to mice, and showed that this substance cannot be the active principle of vaso-dilatin or of peptone. Whether this is so or not, the similarity of their action seems to point to the fact that cutaneous reactions from protein

sensitisation are due, in part at least, to interference with capillary tone.

Nervous Control of the Capillaries.

The evidence of a direct nervous supply to the capillaries is to a large extent bound up with that already mentioned in proof of their independent contractility.

Physiological.—The effect of psychical causes in producing redness and pallor of the skin is well known, and these have been attributed by some observers to an antidromic innervation through posterior root-fibres.

Microscopical.—Histologically it has been shown by Glaser ([19]) and other workers that the capillaries are supplied by nerves. Schafer ([20]), for instance, states that every capillary of the rabbit's mesentery is supplied with a nerve forming loops along it. The fact, recently proved by Krogh, that the capillaries of any tissue are closed until they respond to the requirements of the muscular or metabolic activity of the organ concerned, one capillary, for instance, being closed, while another is actively dilated, seems to me to suggest an independent nerve supply and a possible explanation of the configuration of cutaneous eruptions.

Experimental.—Experimentally, Stricker ([21]), in 1876, found that vascular dilatation, chiefly in the skin, was obtained when the peripheral ends of the posterior roots of the limb plexuses or main nerve-trunks were stimulated. This was confirmed in 1901 by Sir William Bayliss ([22]), who showed that the fibres involved were anatomically indistinguishable from the ordinary sensory afferent fibres, and that they failed to degenerate when the roots were cut between the cord and the ganglion, but degenerated when the dorsal root ganglia were removed. These impulses, which have their origin in the posterior roots, and pass in an opposite direction to the normal sensory impulses, he called "antidromic impulses." He showed, moreover, that it was possible by stimulation of afferent nerves to excite reflex dilatation through the posterior roots, and attributed the effect to an "axon-reflex," the axon dividing to supply one branch to the sensory end-organ and another to the arteriole.

Bruce ([23]) observed that the effect of applying oil of mustard to the skin or conjunctiva was not altered by section of the nerves on the central side of the ganglion, but if the nerve-fibres were allowed to degenerate or were paralysed by local anæsthetics, oil of mustard produced no effect.

Krogh found that the vaso-dilatation which he produced by stimulation of a closed capillary of a frog's tongue with a fine needle was abolished by degeneration of the nerves or the application of cocaine. He states, as the result of his observations, that there is reason to believe that every Rouget cell is supplied from a sympathetic fibre, and can be made to contract through it, confirming the work of Steinach and Kahn as to the presence of a nerve supply to the capillaries in the sympathetic system. He also showed that stimulation of sensory fibres from the dorsal root ganglia causes dilatation of the capillaries as well as the arterioles.

Conclusions.

It is difficult to estimate the relative importance of nervous and chemical factors in the maintenance of capillary tone and their influence on the production of cutaneous reactions, or to draw a hard and fast line between physiological and pathological causes. Cyanosis of the skin, for instance, may be the result of exposure to cold or be due to toxæmia. Livedo reticularis occurs as a physiological phenomenon, or may result from various pathological conditions. The cones of Renaut seem to me inadequate as an explanation of the extraordinary diversity in size and configuration of cutaneous efflorescences—attributed by Unna ([24]) to the inclusion of an increasing number of cones—apart from the independent contractility of the capillaries, and probably also of venules and their vaso-dilator and vaso-constrictor nerve supply from the sensory and sympathetic systems. The formation of wheals, again, may be due to mechanical or nervous influences as in the wheal following the *tâche* which Cotton, Slade and Lewis found in 5 per cent. of their cases, or they may be produced by the application of capillary poisons such as histamine and various products of protein cleavage to the skin. Dale calls attention to the rapid passage of plasma through the endothelial walls when capillary tone, maintained by the contraction of the Rouget cells, is interfered with, and this may have an important bearing on the production of œdema associated with cutaneous eruptions.

In the so-called tropho-neuroses we are probably dealing with capillary dilatation brought about by axon-reflexes. Bayliss and Starling consider that the antidromic impulses of the former observer are concerned in the causation of herpes zoster and other cutaneous phenomena due to nerve injury, and if Cheatle's suggestion regarding the localisation of alopecia

areata and the spreading of rodent ulcer be accepted these would come into the same category.

On the other hand it seems possible that some cases of alopecia areata and localised sclerodermia may be due to irritation of sympathetic fibres.

It is important to remember, as Dale points out, that nervous distribution does not necessarily exclude toxic effects, and that toxins might travel along nerve-trunks from the centre to the periphery as well as in an opposite direction, and this would afford an explanation of the distribution of herpes zoster due to chemical or bacterial poisons.

In conclusion I may say that although the bearing of these facts upon cutaneous disease has not yet been fully worked out, and I am afraid they do not altogether serve to explain the pattern and distribution of cutaneous reactions, they are bound to have a far-reaching influence on our conception of the mechanism by which the latter are produced.

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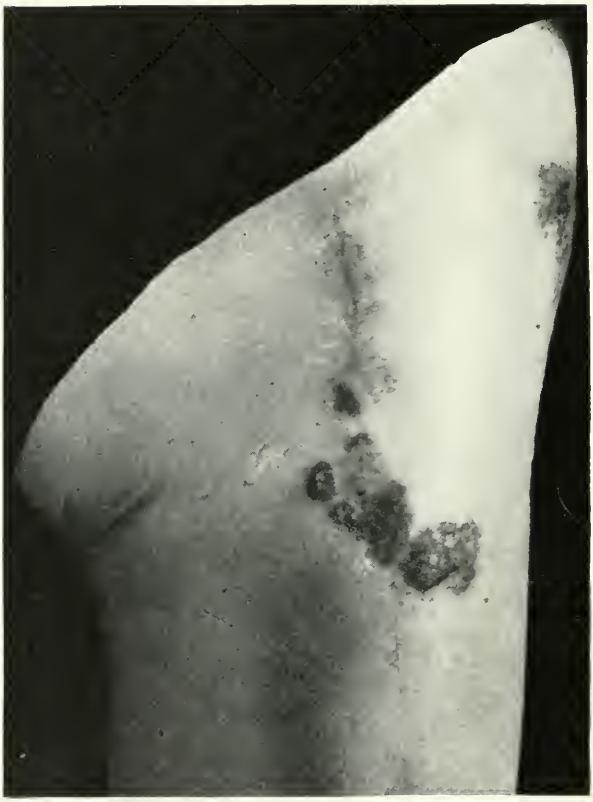

Fig. 1.

TO ILLUSTRATE DR. SAVATARD'S ARTICLE ON PRECANCEROUS DERMATOSIS OF BOWEN.

PRECANCEROUS DERMATOSIS OF BOWEN.*

LOUIS SAVATARD,

Physician to the Manchester and Salford Skin Hospital.

Mrs. C—, a married woman, aged 52 years, consulted me in 1917 for a chronic dermatosis in the region of the right hip-joint. The affected area measured roughly six inches by three. Its centre was occupied by sound white scar-tissue, and surrounding the scar-tissue were numerous red papular lesions, discrete and confluent, some slightly and others more markedly raised above the surface of the skin. They were for the most part covered by slightly adherent scales and crusts. They were firm but not indurated, and did not apparently infiltrate the true skin. Some of the lesions had a slightly warty appearance. On removing a superficial crust a red raw oozing surface was disclosed. There were no subjective symptoms except some occasional soreness.

The history was that the lesion had originated as a red spot on the outer aspect of the thigh thirteen years previously, and that it gradually increased in size till it formed, five years later, a red plaque of the dimensions of a half-crown. At that date her doctor operated, but recurrence was evident at the periphery of the scar-tissue soon after the operation.

Clinically the lesion suggested a probable superficial gummatous infiltration in spite of a negative history. The Wassermann test, however, was negative. X-ray treatment had no beneficial effect, and eventually under the impression of its being tuberculous I scraped the lesions thoroughly and applied a saturated solution of chloride of zinc. The wound healed soundly, but two years later recurrence again occurred at the periphery of the scar, and she returned last September, four years after her former visit, presenting the picture shown in the photograph (Fig. 1).

My colleague, Dr. Gibson, saw the patient on her return, but kindly transferred her to me. We were both struck by the condition's similitude to a serpiginous syphilitic infiltration of the skin, but I remembered there was something peculiar about this case and so turned up my previous notes. This time a small discrete papule was excised for histological

* Read at the Third Annual Meeting of the British Association of Dermatology and Syphilology in Liverpool, July 11th, 1923.

investigation and I found that the section presented a typical picture of Paget's disease, *i. e.* there was marked acanthosis of the rete cells with dyskeratosis, whilst beneath the epidermis the upper part of the corium was invaded by a dense infiltration of plasma-cells and small round lymphocytes. The blood-vessels showed dilatation (Figs. 2 and 3). The clinical picture, however, was not typical of an extra-mammary Paget's disease. It was not vividly red and presented no ulcerated bleeding areas. The lesion, however, was clinically and histologically identical with the two cases of precancerous dermatosis reported by Bowen (1) in 1912. One portion of my section I think shows, too, that malignancy has supervened.

Darier (2) in 1914 reported three other cases which he identified with Bowen's disease, and his third case, a man, aged 65, presented the following lesions :

1. An epithelioma of the forearm of six months' duration, situated upon a large cicatricial surface.

2. Papulo-squamous lenticular lesions scattered over the same cicatricial surface. These lesions had existed for 40 years, and it was their recent transformation that had given rise to the ulcer.

3. A malignant right axillary lymph-gland.

Here, then, we have Bowen's prophecy fulfilled. Darier described many other hyperkeratosic lesions in his cases, but I cannot agree that all these vegetating lesions should either on clinical or histological grounds be identified with Bowen's lesions. I look upon them as simply being associated with such in the same patient. Darier, in his communication, differentiated Bowen's from Paget's disease. I admit, as I have already indicated, that clinically there is not the striking similarity one would have expected from the practically identical histological picture, but I believe that Darier has laid too much stress on the hyperkeratosis present in Bowen's disease. For, if we eliminate the vegetating hyperkeratosic lesions to which I have referred, we do not find a *marked* hyperkeratosis in Bowen's cases nor in the case under review, and further, with all due deference, I submit that Darier's explanation requires further investigation before it can be finally accepted as conclusive. He states further that this hyperkeratosis is made possible in Bowen's disease by the retention of the filaments of union between the rete cells, whereas in Paget's disease the dissolution of these filaments prevents the formation of a coherent horny layer. I have placed under the microscope a section

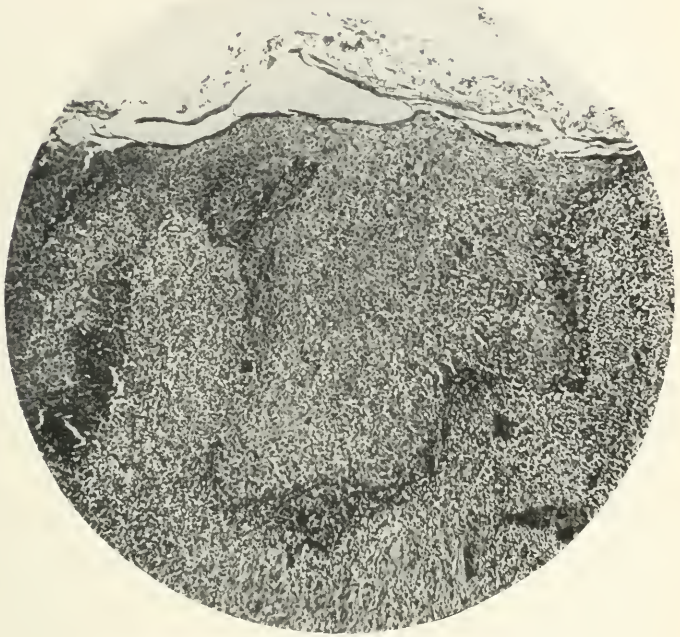

Fig. 2.—Low-power magnification.

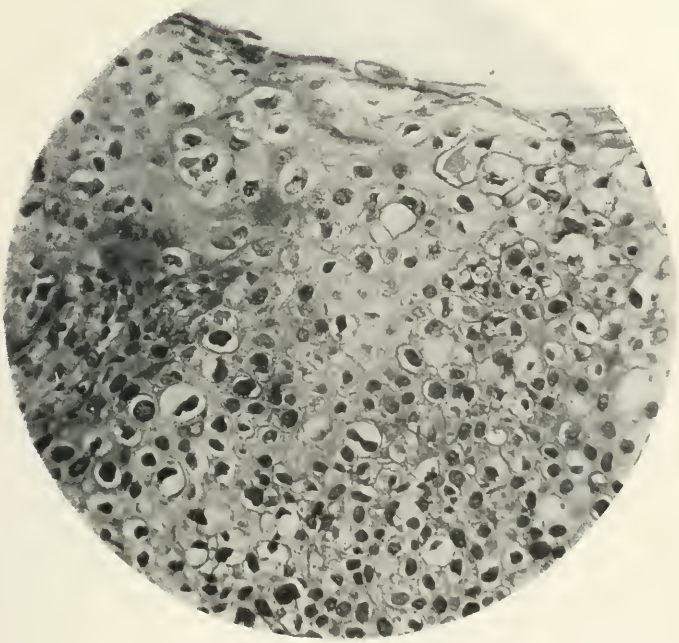

Fig. 3.—High-power magnification.

TO ILLUSTRATE DR. SAVATARD'S ARTICLE ON PRECANCEROUS DERMATOSIS OF BOWEN.

from a case of Paget's disease of the nipple of twenty-five years' duration, on which later a squamous carcinoma developed, and one finds that the prickles are retained, and Macleod (3), in his text-book, seems by his illustrations to emphasise the *retention* of the prickles in the rete cells in Paget's disease. Cannot, therefore, this hyperkeratosis be explained on simpler grounds ? May it not be due to the situation of the lesion ? Is the clinical picture, then, so dissimilar to extra-mammary Paget lesions as to exclude its admission ? I think not. Consider for a moment the varieties met with in lesions of psoriasis, lichen planus, and many other dermatoses. My submission is that the precancerous dermatosis of Bowen is an extra-mammary precancerous dermatosis of Paget.

Walter J. Highman (4) in 1916 reported a case clinically and histologically identical with Bowen's first two cases. The patient was a man, aged 56 years, who for nine years had had an obstinate dermatosis on the right side of his neck. It resembled a crusted tubero-serpiginous syphilide. There was no suggestion of epithelioma. In 1920 (5) Darier reported his fourth case in a man, aged 70 years, who presented a vegetating carcinomatous invasion of the skin of his face (with the exception of the tip of the nose and chin). The cervical lymph-glands were invaded, and, at the autopsy, numerous metastatic growths were found. Histologically the tumour was found to arise from dyskeratosic masses of cells from the surface epithelium, while the secondary growths were the exact replicas of the primary tumours of the epidermis. On account, apparently, of the marked " dyskeratosis " Darier classed this as a Bowen epithelioma, but I believe that this exceptional case is an example of another rare form of carcinoma of the skin which I described here in 1912 under the title of " Sebaceous Carcinoma of the Skin."

In 1915, however, Bowen (6) reported a third case which he considered to be of the same nature as those of his former paper. Although there was marked dyskeratosis, I suggest that the identity is not complete, and his fig. 3 conveys to me the impression that we are here dealing with a case of multiple basal-celled carcinoma, one of which, of thirty years' duration, situated over the right side of the chest, has developed further malignancy.

Whether my surmise is correct or not the report of this case seems to have produced some confusion, and many cases recorded since as of the " Bowen type of *epithelioma* " are in reality cases of basal-celled carcinoma of the trunk. A most illuminating description of this condition is given

by L. W. Ketron (7) in 1919 under the title of "Unusual Forms of Superficial Epitheliomas of the Skin," and a very instructive "abstract of discussion" is appended. His second case was in a man, aged 50 years, who presented on the right cheek a sharply defined oval scar-like area. It was slightly depressed below the level of the surrounding skin and the edge rose rather abruptly. The sunken area was of a pinkish-red colour, soft to the touch and not bound to the underlying tissues. Its surface was rather uneven, and a few pinhead-sized inflammatory papules and crusts were present. The edge was slightly infiltrated and irregular. No raised pearly border was present. This lesion, I think, few of us would have little hesitation in diagnosing as a superficial nodulo-atrophic rodent ulcer; but had it been situated on the trunk, where the crusts and scales are apt to be less frequently removed, it might have presented greater difficulty in diagnosis, and I think if we mentally transposed these lesions from the trunk to the face or forehead, we should realise that they do not differ very materially from many cases we have diagnosed and treated as rodent ulcers. The histological picture of this case showed "degeneration of epidermal cells over cancerous processes." This dyskeratosis, which is not infrequently met with in basal and squamous-celled carcinomas and also in horny papillomas, has apparently been considered by some investigators as evidence of Bowen's disease: for it is only on this hypothesis that I can account for Morrow and Lea's (8) cases being reported as "Two Cases of the Bowen Type of Epithelioma." Mount (9) has even less excuse for labelling his cases of multiple basal-celled carcinomata as of the "Bowen" type.

Martinotti's (10) cases of the pre-cancerous dermatosis are again basal-celled carcinomata, one lesion in the groin of his second case having developed greater malignancy as in Bowen's third case. As a matter of fact this development of a basal-celled into a prickle-celled carcinoma is not so exceptional as is usually supposed, and accounts for many of those prickle-celled carcinomas with a history of some years' duration.

My survey would be incomplete without a brief reference to cases reported and exhibited in this country.

Under the title of "Multiple Carcinoma of the Skin: Precancerous Dermatosis of Bowen," Dr. Sequeira (11) reported in 1921 a most interesting case which presented basal and squamous-celled carcinomata and "pre-cancerous" horny papillomata, but Prof. Turnbull's exhaustive pathological report failed to reveal a single lesion presenting the histological

picture of the precancerous dermatosis of Bowen's early cases. I have placed under the microscope a section of a horny papilloma which, according to Dr. C. E. Jenkins, shows evidence of early malignancy. It shows, too, marked dyskeratosis of the rete cells, but I would not therefore describe it as a Bowen's lesion, though it may be labelled "precancerous."

Some few cases of solitary and multiple "Pagetoid" lesions have been shown at the Dermatological Section of the Royal Society of Medicine within the last two years by Drs. Sequeira, Graham Little, Gray and Savill ([12]), but when Darier was invited in March last to pronounce on these cases he unhesitatingly denied their identity with Bowen's disease, and pointed out that when the latter condition became malignant the glands were involved and the type of epithelioma was a distinct one of its kind.

My last reference is to a case of Paget's disease of the abdomen, exhibited by Dr. W. B. Trimble ([13]) at a meeting of the New York Dermatological Society in November last.

The patient, a woman, aged 63 years, had had a lesion for thirty years, which first appeared on the right side of the navel, and which increased peripherally till, in November, it covered almost the entire right lower quarter of the abdomen. It was superficial, dusky red, and a fine thread-like rolled border could be seen on the inner margin near the midline of the abdomen. The exhibitor stated that histologically it was a basal-celled epithelioma, but that dyskeratotic cells were evident, and therefore he considered the case to be one of Paget's disease rather than plain epithelioma. I can only reiterate what I have already stated—that if we were to examine a large number of carcinomata of the skin we should find dyskeratosis present, but its presence is not evidence of Paget's or Bowen's disease. It was the reading of the last case which incited me to inflict this communication upon you.

Note.

Since sending the above to press, my attention has been directed to a paper by Mlle. Olga Eliascheff in the July number of the *Annales de Dermatologie et de Syphiligraphie* on "De l'épithélioma pagetoide." Her clinical and histological pictures materially confirm my observations and my contention with regard to its differentiation from *pre*cancerous

dermatosis. On the other hand, I cannot agree that there is any necessity for making a separate clinical entity of this type of basal-celled carcinoma.

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SYPHILIS IN THE BECHUANALAND NATIVE: SOME POINTS WHEREIN IT DIFFERS FROM THAT SEEN IN THE EUROPEAN.

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This paper proposes to deal with syphilitic disease occurring in the native population of Bechuanaland, but more particularly among the natives of Taung. It has as its object to draw attention to some points where syphilis in the Bechuana differs from its recognised methods of manifestation in the White Races.

Geographical.

Bechuanaland is a vast stretch of arid veld on the border of the Kalihari Desert. Except for a number of small towns and villages along the railway line running northwards to Rhodesia, and the small township of Kuruman, some 200 miles from Vryburg, it is sparsely populated. Here and there we find a police outpost and widely scattered farm homesteads. The remainder forms a vast stretch of native reserve, occupying the north-western borderland of the Cape Province in the Union of South Africa. It follows, then, that hospital facilities are exceedingly scanty and inefficient, and opportunities for carrying out fruitful investigation have been lacking. Distances are long, transportation non-existent, and communication with the outside world is rare and infrequent. As far as the Government's efforts are concerned, no serious attempt has ever been made to cope with the spread of syphilis in this native domain.

The population of this wide district, excluding Gordonia, was approximately 68,000 at the 1904 census. The races here have not suffered as others have done from the encroachment of European influences and civilisation. On the contrary, the majority still live under direct control of their chiefs, in their kraals scattered throughout their own large native areas, reserved for them by the Imperial Government in the Act of Annexation. As a race they have had everything in their favour under a non-interfering but protective British Government.

Syphilis or Frambœsia Tropica.

In some quarters the doubt has been expressed whether the disease we see in the native in this area, as well as in other parts of South Africa, is syphilis or frambœsia tropica. Arguments in favour of the frambœsia view were put forward by de Vos Hugo, and a fierce controversy raged in the subsequent South African medical press. Since frambœsia tropica has been established as a distinct disease it may be well to settle this point now.

Yaws is a specific disease of the tropics, characterised by a frambœsiform eruption, highly contagious, and generally believed to be due to the *Treponema pertenue* (Castellani). Its geographical distribution is said to include Rhodesia and South Africa (MacLeod). Among Europeans it is exceedingly rare, and is confined almost entirely to natives, where its spread is fostered by insanitary dwellings and overcrowding. While it is most common among children, it may occur at any age. One attack does not produce any absolute immunity, and reinfections are frequent. This is one important point of differentiation between this disease and syphilis. Others of still greater import are that it is not transmitted by heredity, and seldom is seen under six months of age.

The primary stage is characterised by an incubation period of two to four weeks, general toxæmia accompanied by fever, joint pains and headache, an initial lesion of coalescing papules, invariably extragenital, and eventually a dry crust which leaves an ulcer and frequently a granulomatous nodule. The secondary stage appears some six weeks later, and is very much more severe in its general manifestations than the similar stage in syphilis. Crops of tiny papules which eventually form moist warty masses, which dry up and crust, form the typical picture. These crusts, when removed, leave raw papillomatous lesions which are the typical yaws. In old-standing cases the skin exhales a characteristic fusty aroma. Painful ulceration of the soles (crab yaws) with its peculiar gait, nail changes, hyperkeratosis, neuritis and trophic changes complete the picture. The mucous membranes as a rule are peculiarly immune, and adenopathy and eye changes are infrequent. The tertiary stage may appear many years afterwards. Granulomatous ulcers, suppurating gummatous nodules and hypertrophic scarring are most characteristic.

At this point I may quote the summing up of the position as regards Bechuanaland by McArthur and Thornton: "It is, we think, probable that the difficulty in finding initial lesions has been the reason why the

question of the disease being really yaws has been raised. It is hard to understand how any similarity between the two diseases can be claimed. In no way do the symptoms coincide with those of yaws, as recognised elsewhere. There is no regularity of symptoms; there is not the regular age-incidence, the itching, the peculiar smell, or the heaped-up crusts of eruption, and there are very few cases indeed which do not react promptly to mercury in some form. On the contrary, there is the primary sore in certain cases, the adenitis, the exanthem, the alopecia, the bone and eye affections, the polymorphism of the eruptions, and the gummata, and, finally and conclusively, there are the hereditary features of the disease as we see them to-day in these native districts."

Variations in Symptomatology.

After a number of years' experience amongst various types of South African natives, I have long held the view that variations in the manifestations and effects of syphilis exist. Doubtless other observers have noticed these variations, but unfortunately one finds but little reference to the subject in literature. Zimmermann, however, gives an interesting study of syphilis in the negro of Baltimore. He notes the relative infrequency of extragenital infection, the severity of osteo-arthritic manifestations, the frequency of eye symptoms, and the high incidence of follicular and pustular syphiloderms. The annular papular syphiloderm is so common as to reach the dignity of a racial peculiarity. Tertiary bone syphilis is predominant, and the rarity with which neuro-syphilis occurs is emphasised.

There is no doubt that on account of racial peculiarities one meets variations from text-book standards of symptomatology in syphilis. The question naturally arises as to why the disease should show these altered characteristics in native races. It would seem, as a general principle, that the disease attacks the weakest organs—that is to say, those which are submitted to the greatest strain and most active metabolism. It follows that the cerebrospinal axis will be most unlikely to be attacked, and one finds this is so. The digestive apparatus, also, is never severely taxed in dealing with the native's simple diet, and one would be surprised to find severe visceral syphilis. Again this is my experience.

Speaking generally, both as regards acquired and hereditary disease, the severity of the constitutional attack in the native is rarely so severe

as in the European. Malignancy is most uncommon. Constitutional disturbance in debilitated natives and in the bastard coloured races is seen at times, but it is not the rule, and is slight in comparison with the severity of the local lesion. While the actual localised lesion may be exceedingly severe, the general upset is invariably infinitesimal. Thus it is no uncommon incident to find a native with, for example, extensive necrosis and gummatous ulceration of a severity no longer seen in Europe, carrying on his ordinary avocation. Except when inconvenienced or under compulsion, he is quite unconcerned about treatment, and so it will be found with many other severe conditions.

Thus we find the type of lesion in the native varying from that in the European. In addition we also find the utmost variance of the type of lesion, and the course of the disease among the natives themselves. This fact becomes very apparent when dealing with large numbers of cases, and is in itself interesting both in its bearing on the heredo-transmission of the disease, and as a departure from orthodox ideas and accepted clinical standards.

In acquired syphilis one doubtless gets fairly typical stages and symptoms, but it is not at all unusual to find, quite independent of treatment, an irregular sequence of symptoms from the earliest stages. Cases may jump from the initial chancre to a so-called tertiary manifestation. There is, moreover, a constant lapping and concurrence of what in the ordinary way would be called secondary and tertiary symptoms.

One also meets a type of case where it is difficult, and indeed often impossible, to say whether the disease is acquired or hereditary. In cases presumably acquired, one finds constantly exhibited stationary conditions of the lesions such as one finds in heredo-syphilis. On the other hand, the latter class, at all ages, may exhibit lesions indistinguishable from those which might have been acquired in origin. This variation in symptomatology leads to difficulty in differentiating between the two types. From my observations some of the more interesting points in these features of native syphilis are these :

(1) Absence of visceral lesions.
(2) Absence of neuro-syphilides.
(3) High incidence of *syphilis hereditaria tarda*.
(4) Chronicity of isolated lesions.
(5) A favoid condition of the scalp and its relation to syphilis.

(1) *Absence of visceral lesions.*—This is quite an evident feature in these

people as in other native races. With an experience of a large number of post-mortem examinations among natives, I have not yet found a gumma of the viscera. The remarkable integrity of the viscera in native syphilis perhaps accounts for the continued virility of these natives under aggravated conditions of disease, which would prove incapacitating or even fatal to the European. Not only do they carry on their usual avocations, but propagation is unhindered, and seldom interrupted by abortion or miscarriage. Active lesions in the female do not seem to foster miscarriage. So it follows that these natives are assured of offspring, which, after all, is the supreme ambition of their existence.

Since Brock drew attention to a lung condition which he found frequent among syphilitic South African natives, I have particularly investigated this point. He described a particular apical affection which he found in 35 per cent. of his cases, but I have not found such a lesion in anything like the proportion that he reports. I agree, however, that there is a marked tendency to lung affection. This I have observed for a very long time, the usual lesion being of the character of an interstitial fibrosis of irregular distribution and situation. Various post-mortem examinations on natives often have revealed, with and without known luetic histories, signs of old pleurisies and fibroid changes in the lungs, sometimes accompanied by small healed cavities. I have, however, had no opportunity of observing changes at autopsy in a case where the lung condition had been active at the time of death. I am satisfied that in native syphilis there is to be found at times a not very active form of specific pulmonary fibrosis.

Colleagues in neighbouring districts have had similar experience—a fact which is of considerable importance in connection with the spread of native tuberculosis. The native suffering from syphilis, whether it be hereditary or acquired, is prone to develop tuberculous pulmonary lesions, either with a slow, insidious onset most frequently seen in syphilitics of long standing, or with an acute and rapidly fatal course, which occurs in the more severe types of naso-pharyngeal and laryngeal syphilitic lesions.

I have found much evidence of this latter condition at autopsy in cases where death had occurred from hæmoptysis. No doubt the pulmonary fibrosis is a factor in determining this fatal termination. Pulmonary tuberculous disease is making rapid strides among the native races in South Africa, in spite of favourable climatic conditions, and the

significance of syphilis as a predisposing ætiological factor should not be overlooked. There is ample evidence of this already among the degenerates of the bastard half-breed races of South Africa. The history of their syphilisation dates back to the early days of coastal settlement, and their susceptibility to pulmonary tuberculous disease is a fact well recognised. It would indeed be a short-sighted policy to ignore the possibilities of broadcast tuberculous infection taking place among those native races, already degenerate, now in process of syphilisation.

(2) *Absence of neuro-syphilides.*—Implication of the cerebro-spinal axis in the native is practically unknown. I have met with only six cases with pronounced nervous lesions and tabes dorsalis and dementia paralytica have never been seen. This rarity of neuro-syphilis among native races has been previously noted, and various speculative reasons have been advanced in explanation. Those usually mentioned are the absence of alcoholism and freedom from nerve-strain. In old-time European syphilis, the incidence of nerve symptoms was indirectly proportional to the severity of tertiary lesions. It is a fact, as one would anticipate, that the so-called tertiary stage in the Bechuana is uncommonly severe and destructive, while the deep viscera and cerebro-spinal axis apparently escape. The incredible amount of heredo-syphilis would suggest that there is no exhaustion of the virus, and little in the way of immunisation, either relative or absolute. This is possibly due to the fact that the process of syphilisation started so recently in the history of the races concerned.

Freedom from alcoholism as a probable explanation of the apparent immunity of the cerebrospinal axis does not carry us very far. In these parts alcohol is the bane of the native's life. He indulges over-freely in the beer he brews—a beverage by no means impotent—and this he strengthens still further on every possible occasion with foreign spirit. In the towns, or whenever opportunity occurs, his main object is to get systematically drunk.

Again, it is not enough to suggest that the disease among these people is benign, or that they show unusual tolerance to the disease. They have failed to show tolerance to many other diseases, such as smallpox, while they have successfully acquired the European's partial immunity to measles and scarlet fever.

It is generally acknowledged that the *Spironema pallidum* is prone to attack weakened tissues. The European certainly uses his central

nervous mechanism more than does the native, and the bustle of modern civilisation possibly adds to the general strain to which the European's cerebrospinal axis is submitted. It would appear, then, that this circumstance might explain the immunity of the native to cerebrospinal syphilis. That it is only part of the explanation, however, is clear on further inquiry. Other factors materially affect the issue, chief of which is the question of antibody formation. For many years native syphilis was absolutely untreated, and even at the present time there are vast numbers of infected natives, chiefly in the native reserves, who receive no treatment at all, or at best only scanty and inadequate medication. Moreover, where treatment has been carried out systematically, it has consisted solely of mercury and potassium iodide. These drugs, as we know, do not inhibit antibody formation, and these patients have been flooded with a plentiful supply of antibodies over long periods of years, which apparently have proved sufficient to guarantee the adequate protection of the cerebrospinal axis. The cerebrospinal axis has been bathed in antibodies since the early days of the primary infection, and any stray or enterprising parasite has been afforded little opportunity to do harm. This fact, if taken into consideration together with the previous statement that the cerebrospinal axis is intact and has at no time been submitted to strain of any kind, may be sufficient to explain the immunity of the central nervous system in spite of (or rather, perhaps, in virtue of) the extreme destructive severity of the so-called tertiary cutaneous lesions. Even there, however, the lesions are peculiarly localised, and Nature's efforts at tissue repair are truly wonderful.

That treatment methods afford a large part of the explanation is further borne out by the experience of Mehliss, to whom is accredited the statement that neuro-syphilides of even the mildest variety have only appeared among South African natives since the introduction of arsenobenzene into the treatment routine. If, therefore, the arsenobenzene-treated native is liable to exhibit a neuro-syphilide, we have strong additional evidence that the type of treatment has much to do with the determining of the negligible incidence of cerebrospinal syphilides. In view of the work of Wile and Stokes, who declare that the fate of every syphilitic as regards his cerebrospinal future is determined in the first months of the infection, an investigation into spinal fluid changes in early native syphilis would be exceedingly instructive. Reith Fraser sums up the position as follows: "In the natives of South Africa the mild primary

stage which is characteristic, and which is frequently absent, is due to a lack of local cell reaction around the attacking organism, and not to any inherited immunity. The cell reaction is seen in the generalisation stage when cutaneous syphilides are particularly severe. The antibody mobilised at this period seems to act as a bulwark of defence for the nervous system, which subsequently is never involved to an extent sufficient to produce clinical symptoms."

(3) *High incidence of syphilis hereditaria tarda.*—The vast amount of hereditary syphilis is one of the most striking features of native syphilis in Bechuanaland. Speaking generally one is most impressed with the puny condition in infancy of syphilitic children as compared with the youth of non-syphilised tribes. This leads in after life to a degree of arrested development not amounting to infantilism, but effecting a marked diminution of physique. There is no constancy in appearance of the many text-book signs of heredo-syphilis. One may look in vain for " the triad of Hutchinson." Keratitis is seen occasionally, but specific deafness is unknown. Hutchinson's teeth simply do not exist, but Wall's mulberry molar is met with in practically every case (Reith Fraser). The " saddle nose " is often in evidence, but then that is also a type of physiognomy. Amongst the more frequent manifestations are mucous plaques, condylomata, tibial periostitis, and " wit kop "—a favoid condition of the scalp, which will be discussed later.

I have found that irregular outbreaks of hereditary syphilis occur in families at any period from infancy even up to full adult and marriageable age. In fact I have suspected that many cases appearing at later periods verging on middle life are instances of *syphilis hereditaria tarda.*

The evidence of any former lesions is quite uncertain in cases of late heredo-syphilis. In some it will be found, while in others it is definitely absent. When such evidence is present it is rare to find that there has been any previous treatment. There is no doubt that in such cases, with signs of lesions in infancy or early youth, the condition went on spontaneously to latency. In others a clinical cure would seem to have taken place. Of this I have numerous examples.

In many families there is no direct parental history. This may be considered strange and unlikely, but the fact that maternal syphilis is so frequently latent and symptomless must not be forgotten. In spite of this, however, the vast majority of such cases must be considered examples of *syphilis hereditaria tarda* for these reasons: (1) lack of evidence of

acquired infection, and (2) the discovery of other members of the family showing active lesions at some later date. Whether there is a parental history or not the similarity of symptoms in such cases is very striking. It is therefore impossible to ignore the question of hereditary infection in explaining these irregular outbreaks of syphilis in families.

In spite of the exceedingly high incidence of heredo-syphilis abortions and miscarriages are rare, and infant mortality is in no way abnormal. The acquired and the hereditary syphilitic marry and are given in marriage. It is more or less an everyday occurrence for a hereditary syphilitic to marry a syphilitic, also hereditary; for an acquired syphilitic to marry an acquired syphilitic; for a hereditary syphilitic to marry an individual who has acquired his disease; and for a healthy normal individual to marry a syphilitic, either acquired or hereditary. In spite of this alarming state of affairs these people propagate with regularity, commendable frequency, and precision. Their children are syphilitic, they grow to maturity, and proceed to do likewise. Thus we are faced with the problem, not of sôlving the result of introducing a syphilitic genitor into a healthy family tree, but of introducing an acquired or hereditary syphilitic into a family tree already well syphilised! We find examples of hereditary syphilitics inter-marrying throughout three or four generations, where it is quite the exception to have an untainted or an acquired syphilitic genitor introduced. In spite of this syphilisation going on through generations, the fœtus successfully manœuvres his intrauterine life, and comes out in the open a full-blown syphilitic who can boast of his spironemal history going back three or more generations on both his paternal and maternal sides, without the blemish of an untainted healthy ancestor. Moreover, he develops as a pathognomonic heredo-syphilitic should, and shows a generous proportion of the signs and symptoms of his kind. In turn he marries a heredo-syphilitic mate, and their children present similar luetic characteristics. In other words, the passage of generations may serve to modify the disease, but it does not stamp it out.

In the face of such evidence one must certainly ponder over the possibilities of third generation transmission. As has been pointed out, there are plentiful examples of long-standing lesions in heredo-syphilitics, and also numerous instances of latent heredo-syphilis. Lesions thus will be found to be active and virulent at the procreative age, and the possibilities of offspring from such parents is undoubted. Indeed, living

offspring from such parents have been met with frequently in one's own experience.

According to Tarnowsky many of these cases would probably be regarded as examples of "binary syphilis." I have been unable, however, to obtain any evidence of reinfection. We have to admit a certain amount of laxity in native domestic life, but with the wide-spread disease which is encountered one would also have to suggest nothing short of wholesale immorality to account for the reinfection of these numerous heredo-syphilitic genitors. I am aware that it is not easy to disprove reinfection, but some evidence must have been forthcoming, and yet I cannot note even a suspicion of this having occurred amongst all the cases which have passed through my hands. Another point which has to be borne in mind is that native syphilitics do not bear out some of the most important conclusions of Tarnowsky, regarding the possibilities of third generation transmission. There is no evidence of heredo-syphilis being responsible for much abortion, miscarriage or still-birth. The dystrophic effects of hereditary syphilis are very variable, and often are absent. Moreover, there is no marked intensity of symptoms in the second generation. The objection that hereditary syphilitics with active disease are unlikely to marry does not apply to the native. Such an actively infective parent may propagate children showing active or latent syphilis, and it is certain that infant mortality among such progeny is by no means excessive. We must remember also that the disease has existed for many years in these districts, and is practically untreated. Yet there is no evidence to show that there is any appreciable diminution of the population from its effects, or, what is more crucial, the evidence of sterility and dying out of families, and an increasing infant mortality.

Constitutionally, as has been shown, the native does not suffer as the European. He maintains his virility in spite of the most destructive lesion, and with good food and a little nursing he will often be able to rid himself of an active lesion without the aid of any specific treatment whatever. This was proved by a parallel series conducted at the Kimberley General Hospital by Russell.

It is difficult to see how the possibilities of third or subsequent generation transmission are to be denied. Even the possibility makes one regard the future of the Bechuanaland native with apprehension.

(4) *Chronicity of isolated lesions.*—It is a common occurrence for adults of all ages to be placed under treatment with such conditions as advanced

naso-pharyngeal ulceration of many years' duration, showing little more than a very slowly progressing tissue destruction. Amongst other single manifestations frequently met with are grouping of various forms of pustular syphilides about the elbows, knees, thighs and buttocks. The latter is a particularly favourite situation, and the pustules are generally implanted in a mass of gummatous tissue. There are also to a lesser extent other lesions exhibiting a similar isolation and chronicity. These isolated lesions are found to have existed for years; they are so slightly progressive as to be almost stationary; they give rise to little inconvenience; bodily health is unimpaired: there has been no treatment of any kind in the majority of cases, and there have been no concurrent lesions. There are also more youthful cases, undoubtedly hereditary, which will be found to exhibit a similar chronicity and isolation of lesions.

Investigations as regards the adult cases point to this peculiarity of manifestations as being more of a feature of heredo-syphilis, for there is to be obtained the evidence of lesions which have occurred at quite youthful ages. In particular, there are two which are very distinctive, namely, signs of an old "wit kop" and the deep scarring left by former mucous plaques. With or without such signs there is often a history of "sores" in youth. In contradistinction to the latter, one comes across a certain number of cases with old chronic lesions which give a clear history of an earlier acquired origin, previous treatment, other lesions and healed conditions. There are, however, the numerous instances with no history to guide one, and the question to be solved is whether one is dealing with hereditary or acquired disease. In the younger and known hereditary cases one meets the same conditions of long-standing lesions. The comparison makes me strongly of opinion that most of these doubtful adult cases are in all probability examples of *syphilis hereditaria tarda*.

I am aware that a condition such as described, when met with in adult natives living in towns, is classed usually as a secondary or tertiary manifestation of acquired syphilis. In a rural district, however, there is every opportunity of studying family history—a privilege denied to the town worker. Moreover, there is also to be found the exact similitude of secondary and tertiary lesions in the native heredo-syphilitic of all ages. Personally one does not meet with many cases having a clear history or evidence of acquired disease, early or late, and it is a remarkable fact how very few primary lesions are ever seen amongst these people.

The migration of natives from country to town and *vice versâ* is continual, and in view of the vast amount of acquired syphilis in towns there should be ample evidence of primary infection among the natives under review. I do not deny that such is to be found there, but consider that all doubtful cases must be regarded as hereditary in nature, more especially if they should come from a known syphilitic family.

A study of the progeny of syphilised families is instructive. It is soon apparent that the children of the acquired syphilitic are most actively affected, and show a high death-rate in infancy and youth. Such families, however, are very much in the minority. The children of families syphilised in previous generations show much irregularity in the type and date of onset of symptoms. Many members of such families show definite clinical signs of syphilitic infection sooner or later, while others remain clinically quiescent. Among the heredo-syphilitics showing clinical manifestations in early life, the chronicity of individual lesions is especially marked, and it is rare to see any of this class showing rapid development of the disease. Tissue destruction may be extensive and disfiguring, but it is never rapid. This is in marked contrast to the untreated acquired syphilitic in the so-called tertiary stage of the disease.

Considering all these points I cannot but incline to the belief that this peculiarity of manifestation is associated with hereditary disease, and not with that which is acquired. I may cull as additional evidence the fact that acquired syphilis as seen in the town native presents a typical primary genital focus, characteristic secondary exanthem with certain racial peculiarities, and a text-book tertiary stage with extensive and rapidly destructive cutaneous and bony lesions showing their typical tendency to relapse. Since the general employment of arsenobenzene medication, also, we have much evidence that the native is now exhibiting active implication of his cerebrospinal axis.

(5) "*Wit Kop.*"—There are some interesting features in the condition about to be described which make it worthy of special remark. The attention of the medical profession in South Africa was first directed to this condition by McArthur and Thornton in 1910, and an excellent description has been given by Reith Fraser in the *British Journal of Dermatology and Syphilis.* It is a syphilitic condition of the scalp, most frequently seen in hereditary syphilis, but occasionally met with in the acquired disease, which resembles impetigo in its early stages, but more closely simulates favus in its fully developed state.

The first evidence of the condition is the appearance of one or more discrete, white "scurfy" spots on the scalp. On minute examination a small immature indurated papule will be found. There is no congestion, hyperæmia, or inflammatory reaction. Gradually other similar spots appear; they cease to be discrete and coalesce with the formation of heaped-up crusts. These in turn coalesce into large patches until the whole scalp is finally involved. At this stage the patient looks as if he were wearing a tightly-fitting white cap showing a slight fringe of hair at the lower margins. The condition is well known to the native, and goes by the name of "wit kop" (white head) or "dikwakwadi."

The age-incidence is from infancy to late puberty, but its incidence in Bechuanaland is greatest between the ages of 2 and 10 years. While it is seen most frequently as a manifestation of hereditary syphilis among these people, it has been known to occur as a secondary lesion in acquired syphilis. Quite recently Reith Fraser has had several such cases under his care in the New Somerset Hospital, Cape Town. With him I encountered several early cases among reformatory native boys in the Cape Peninsula.

This favoid condition is frequently associated with mucous tubercles and condylomata. One generally finds that there is abnormal rhinitis present. It is not uncommon to find a congested and often petechial area around the mid-line of the hard palate. Accompanying this there may be some œdema of the nasal mucosa. These symptoms are invariably the precursors of the severe destructive lesions of the naso-pharynx so common among these peoples, and so frequently a sequela of the more chronic cases of this favoid syphilide.

Recapitulation.

Hereditary syphilis is by far the most frequent type of this disease met with in Bechuanaland. Acquired syphilis occurs, but it is comparatively rare. The chancre is seldom seen, and as often as not is extragenital.

There is much presumptive evidence that the possibility of hereditary transmission to the third generation is a very real thing. The rarity of acquired infection is an important point in deciding the issue, together with the very wide-spread syphilisation of whole families.

The absence of visceral syphilis capable of producing clinical signs is noteworthy. It is accounted for chiefly as a racial peculiarity, possibly

resulting from the untaxed state of the native's digestive apparatus, his slow rate of metabolism, and the strain-excluding, easy-going, open-air existence which he leads.

The prevalence of a specific pulmonary fibrosis is not so great as has been suggested by other workers in other parts of South Africa. Brock concluded that 80 per cent. of natives show a fibroid condition of the lungs, or an indurated enlargement of the epitrochlear gland, or both, and that syphilis is responsible for both of these conditions. In laying a pulmonary fibrosis in 35 per cent. of natives to the charge of syphilis, particularly among natives engaging in work in the dust-laden air of the Rand Gold Mines, I am of opinion that his figures greatly exaggerate the position.

The absence of neuro-syphilides among coloured races has frequently been recorded. This phenomenon is observed in Bechuanaland. The fact that the native's cerebro-spinal axis is not submitted to the strain and worry of modern civilisation may be part of the explanation. Much more important seems to be the antibody supply which he receives from his general systemic circulation, which is constant and prolonged over an indefinite period. This antibody supply is at hand when any spironemata are advancing to the attack, and clinical signs fail to supervene.

The very high incidence of *syphilis hereditaria tarda* is particularly striking. It is accompanied by a very small incidence of abortions and miscarriages, and a low infant mortality. Whether this occurs most frequently in second, third, or subsequent generation heredo-syphilis, or in generations where there may be a normal individual, an acquired syphilitic, or a heredo-syphilitic on either side in the previous generation, is quite uncertain.

The typical chronic and comparatively non-destructive course of isolated lesions is characteristic of native syphilitic disease met with in Bechuanaland, but particularly so of *syphilis hereditaria tarda*.

"Wit-kop," a favoid condition of the scalp, is characteristic of heredo-syphilis in Bechuanaland, but it has also occurred coincident with the secondary eruption in native acquired syphilis elsewhere. It has not yet been met with in a European or in a native non-syphilitic. A fungus which apparently flourishes on scalps so affected has been suggested as the causal factor. The overwhelming bulk of evidence, however, goes to indicate that "wit-kop" is spironemal in origin.

I take a very real pleasure in acknowledging the encouragement and

practical assistance I have received in this work from Sir Edward N. Thornton during the years when his departmental activities brought him to Bechuanaland. My thanks are also due to Dr. A. Reith Fraser, Cape Town, for his generous assistance and numerous suggestions in the preparation of this paper.

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THE LONDON SCHOOL OF DERMATOLOGY.

For many years the lack of a central post-graduate school in Dermatology in London has been much felt, and from time to time endeavours have been made to form some such school in connection with one or other of the special hospitals for skin diseases, but without success. Within the last few months, however, a further attempt was made in this direction, and this time with success. Thanks to the goodwill of the Board of Management and the Medical Staff of St. John's Hospital for Skin Diseases, Leicester Square, a central School of Dermatology has been started in which the teachers comprise, not only the staff of St. John's Hospital, but also the heads of the dermatological departments of the twelve London Medical Schools. The staff of St. John's Hospital has been augmented by the election of Sir Malcolm Morris and Dr. J. H. Stowers to the Consulting Staff, and of Dr. Wilfrid Fox and Dr. Henry MacCormac to the Visiting Staff, and Dr. J. M. H. MacLeod has been

appointed Director of the Pathological Department. Dr. M. G. Hannay has undertaken the arduous duties of Dean. A programme of lectures for the first six months of the present academic year has been drawn up, and the first few lectures have already been delivered.

We feel convinced that this step will lead to a great improvement in the position of London as a teaching centre in this special branch of medicine. In the past it has been a matter for complaint among visitors to this country that they had to go from one hospital to another in order to fill in their time, whereas in Paris, Vienna and other continental cities they could obtain continuous instruction at one central clinic. London will now come into line with these other famous centres of dermatological teaching, and in addition, for those interested in special work, the clinics of the large teaching hospitals will still be available.

The credit of carrying out the somewhat delicate negotiations which preceded the formation of the School is due to Dr. J. H. Stowers, and in order to congratulate him on the success of his efforts he was entertained at a complimentary dinner on October 10th by the staff of the School, at which Sir Malcolm Morris presided.

We feel that we shall be voicing the sentiments of all those interested in British Dermatology in wishing the School every success.

CURRENT LITERATURE.

INFLAMMATIONS, ETC.

ANGIONEUROTIC ŒDEMA WITH ADENOPATHY. Z. Moravec. (*Česká Dermatologie*, 1923, iv, p. 91.)

Following ingestion of fish a 12-year-old boy developed severe œdema of the face, neck, and upper part of the chest with enlargement of submaxillary, preauricular and parotid glands, a generalised urticaria rosea hæmorrhagica, acute œdema of larynx and acute pulmonary œdema. Albumen was present in the urine, and the temperature was 39·2° C. The findings cleared up in a week under thyrotoxin. Spinka (St. Louis).

CONTRIBUTION TO THE QUESTION OF THE TREATMENT OF PSORIASIS. H. E. Ahlswede and W. Busch. (*Urol. and Cut. Review*, January, 1923.)

The treatment outlined is based on the idea that psoriasis is an infectious skin disease, and the object of the treatment to increase the natural resisting powers of the body. The method is as follows: 2 c.c. of patient's blood is

withdrawn from a vein and immediately injected subcutaneously or intramuscularly. Every third day thereafter 1 c.c. of 10 per cent. solution of quinine bisulphuride is injected subcutaneously.

Simultaneously the psoriasis areas on the skin are treated with high-frequency currents to cause slight hyperæmia. No mention is made about the duration of treatment.

The purpose of the method is to cause a local hyperæmia in the affected skin and to inject a bactericidal agent—namely quinine. W. H. B.

CLINICAL ERRORS IN THE DIAGNOSIS OF ACUTE CONTAGIOUS DISEASES. Litchfield and Dembo. (*New York Med. Journ.*, March 7th, 1923, p. 257.)

The authors discuss the signs and symptoms of measles, diphtheria, scarlet fever and chickenpox. They lay especial stress on the interpretation of the rashes, and point out the errors that may be caused by the administration of various drugs (such as bromides, antipyrine, salicylates and chloral) in the very early stages of the disease before the normal rash has appeared. Serum rashes also receive attention, and are stated to appear from one day to "several weeks" after injection. The differential diagnosis of variola and varicella is also discussed. W. F. C.

MYCOSES RESEMBLING ECZEMA. C. Rasch. (*Acta Dermato-venereologica*, iii, 3–4, p. 311, December, 1922.)

An interesting survey of the author's own observations is accompanied by some useful photographs. The cases are classified as (*a*) epidermophytia inguinalis (Sabouraud), (*b*) trichophytia resembling eczema, and (*c*) eczema or eczema-like cases due to yeasts. Particularly interesting is the description of three cases of yeast mycoses in infants. Rasch takes care to point out the non-proven pathogenicity of the yeast fungi in such cases. As a local application ung. chrysarobin ½–1 per cent. or ung. anthrarobin 1 per cent. is preferred to iodine or to Whitfield's ointment. W. J. O.

DERMATOSIS DYSMENORRHOICA SYMMETRICA. Polland. (*Derm. Zeitschr.*, April, 1923, p. 89.)

Polland brings forward fresh evidence in favour of the authenticity of the disease described by Matzenauer and himself under this title. He emphasises that his dermatosis can be differentiated from autophytic eruptions by its symmetry and by a careful study of the whole course of the lesions, not merely of one phase of them. All attempts to produce similar lesions experimentally have been unsuccessful. A number of new cases recorded by various authors are set out and closely discussed. J. F. S.

MUCOUS MEMBRANE CHANGES IN PITYRIASIS RUBRA PILARIS. Jordan. (*Derm. Zeitschr.*, May, 1923, p. 257.)

Jordan describes a case of pityriasis rubra pilaris in a woman, aged 30 years, on whose palate were two whitish, linseed-sized, slightly raised lesions. A biopsy of one showed changes considered characteristic of the disease, and this opinion was strengthened by the fact that the other underwent regression *pari passu*

with the skin eruption under intensive arsenical treatment. He has found two similar cases in the literature. J. F. S.

LUPUS ERYTHEMATOSUS. F. Gardiner. (*Edin. Med. Journ.*, 1923, xxx, 6, p. 233.)

Case reported of female, aged 18 years, with her face and hands affected. Cervical glands were enlarged, as was also her left tonsil. She was admitted into hospital with a temperature of 102° F., and died 10 days later. Sputum was rusty as in pneumonia. Blood cultures were negative. Post mortem many organisms were found in the lungs, including diphtheroids, pneumococci, *M. catarrhalis*, Gram-positive cocci and streptococci. The lungs showed acute pneumonia and tuberculosis. Tuberculous adenitis was fairly general. The spleen showed many tuberculous foci. The blood taken from the heart grew a streptococcus.

Out of the author's last 33 cases, 27 were female and 6 male: 9 showed old tuberculous scars, 14 had a definite focus of septic teeth, 10 an equally septic tonsillar condition; 9 blamed local injury, such as septic sores, midge-bites, or exposure to heat or bright light; 6 gave a definite history of rheumatism.

The author concludes that lupus erythematosus is probably not a definite clinical entity. W. F. C.

APLASIA MONILIFORMIS. James Strandberg. (*Acta Dermato-Venereologica*, iii, 3–4, December, 1922, p. 650.)

Short commentary based on the observation of two sisters with monilethrix, keratosis pilaris and defective development of the permanent teeth of a family including, in three generations, five members who showed defective development of the teeth and hair, which is presumed to be an expression of endocrine deficiency. W. J. O.

ERYTHRODERMIA DESQUAMATIVA (LEINER). Fr. Grön. (*Acta Dermato-Venereologica*, iii, 3–4, December, 1922, p. 451.)

Ten cases are reported (6 males, 4 females), of which 2 died (1 with intercurrent diphtheria, 1 with disease in question). Post-mortem examination in both cases revealed normal stomach and intestines without any sign of gastro-enteritis. Of this series, 6 had been exclusively breast-fed both before and also in some cases after the appearance of the skin affection. Two private cases continued to be breast-fed during the whole period of their disease and up to 7 and 9 months respectively. In 5 cases diarrhœa with fluid slimy stools had been noticed before the onset of the skin disease; in the remaining 5 cases there had been no alteration in the fæces. The conclusions drawn are that Leiner's disease is a characteristic dermatosis of unknown ætiology, distinct from Ritter's exfoliative dermatitis but allied perhaps to generalised seborrhœic eczema, and that the condition may occur in both breast-fed and artificially fed infants, accompanied often, but not invariably, by evidence of some disturbance of the alimentary tract. W. J. O.

THE BENEFITS OF ORGANISATION IN THE TREATMENT OF LUPUS. R. Aitken. (*Edin. Med. Journ.*, 1923, xxx. No. 7, p. 117.)

A special lupus clinic has been arranged in Edinburgh, and it is found that this encourages patients to attend regularly over long periods of time as they feel that especial interest is being taken in their cases.

Wassermann reactions were taken in sixty-three patients; of these five were returned as positive: all the remainder were negative.

The treatment used for lupus included carbolic acid, trichloracetic acid, lactic acid, acid nitrate of mercury and X-rays. Cases in which the catarrhal element was well marked were scraped with a sharp spoon and a staphylococcal vaccine given. Treatment with tuberculin is carried out in a large number of cases, the injections being given weekly or fortnightly. The author believes very strongly in the tuberculin treatment, and gives a list of clinical cases who have benefited by this treatment. W. F. C.

ARTIFICIAL LIGHT TREATMENT OF LUPUS. Axel Reyn. (*Brit. Med. Journ.*, 1923, ii, p. 499.)

A paper read before the annual meeting of the British Medical Association, in which the treatment of surgical tuberculosis is also discussed. Before proceeding to the matter of general light-baths, Finsen's local treatment is first briefly reviewed. Details of the apparatus used for the light-bath treatment are then given. The carbon arc is preferred as a source of light, as it contains all the rays of the spectrum, together with the long-waved ultra-violet rays which alone penetrate the epidermis. The mercury vapour arc light gives off chiefly only the short-waved ultra-violet rays. Further details as to the duration of exposure are then dealt with. The author insists on the importance of combining local with the general treatment, and claims 90 per cent. of cures when these are efficiently administered.

J. H. Sequeira. (*Brit. Med. Journ.*, 1923, ii, p. 503.)

The author entirely agrees with Prof. Reyn both with regard to the importance of combining local with general treatment and in the matter of the percentage of cures. He further points out the differences in treatment required by the dry and ulcerative forms of lupus, as well as describing the effects on the general health of the patient. M. S. T.

ERYTHÈME NOUEUX FAMILIAL. P. Woringer. (*Journ. de Méd. de Paris*, 1923, xlii, 12, p. 241.)

The ætiology of erythema nodosum is briefly discussed, and a case is reported which the author suggests took the course of a definite infectious disease comparable to the eruptive fevers.

A girl, aged 9 years, had typical erythema nodosum with rise of temperature eight days after a mild sore throat. A brother, aged 12 years, had an exactly similar condition occurring two days later. In the boy's case there had been no history of sore throat, but there had been an attack of abdominal pain eight days before the eruption. Other similar cases are quoted from the literature.

M. G. H.

FRAMBŒSIA TROPICA. Gislen. (*Arch. Med. Belges*, 1923, lxxvi, 6, p. 464.)

After briefly mentioning some of the usual characters of the disease, the author suggests that there is a tertiary stage. He mentions cases of iritis, ulceration of the naso-pharynx, and symptoms resembling tabes and G.P.I. which he regarded as due to frambœsia. Congo syphilis has the reputation of being benign, and the suggestion is made that this may be due to cases of pain being mistaken for syphilis. M. G. H.

XANTHOMA AND HYPERCHOLESTERINÆMIA. William H. Mook and Richard S. Weiss. (*Arch. of Derm. and Syph.*, 1923, viii, p. 19.)

In this paper three cases of xanthoma diabeticorum and three cases of xanthoma tuberosum are reported in detail. It was found that the cholesterin content of the blood was markedly increased in the xanthoma diabeticorum cases, that it was also markedly increased in two of the xanthoma tuberosum cases, while in the third tuberosum case, which was associated with general arteriosclerosis and hypertension and myxœdema, it was only slightly increased.

Excluding the palpebral type, the writers believe that the xanthomas belong to the class of foreign-body tumours; that they are a connective-tissue cellular reaction to the deposition of cholesterin bodies from the blood in cases in which a hypocholesterinæmia is present; that they are localised by motion and trauma.

J. M. H. M.

THE WASSERMANN REACTION IN LEPROSY. John A. Kolmer and Oswald E. Denney. (*Arch. of Derm. and Syph.*, 1923, viii, p. 63.)

In a series of 159 cases of leprosy, clinical or serological evidence of syphilis was found in 27, or 17 per cent. In those cases the positive Wassermann reaction was due to syphilis and unconnected with leprosy. In non-syphilitic lepers, with an old technique, similar to the original Wassermann method, apparently positive results were obtained with 7·2 per cent. of the serums, but when these were tested by a new technique the reactions were uniformly negative. In this new technique devised by Kolmer a new antigen is employed, consisting of a cholesterinised alcoholic extract of heart muscle (*Amer. Journ. of Syph.*, 1922, vi, p. 74), and a primary incubation of eighteen hours at 6° to 8° C., followed by ten minutes in a water-bath at 38° C., and technical improvements including the routine titration of complement in the presence of the antigen.

Since this new complement-fixation reaction does not yield falsely positive reactions, it is of value in differentiating between leprosy and syphilis.

J. M. H. M.

LICHEN NITIDUS. H. E. Michelson. (*Arch. of Derm. and Syph.*, 1923, vii, p. 763.)

A typical case of this, affecting the wrists and cheeks, in a medical student is here described. The lesions were of the characteristic type and closely resembled the plain type of Lichen scrofulosorum. Histologically the lesion is a sharply defined granulomatous mass made up of round-cells, epithelioid cells, fibroblasts and giant-cells. There was no positive evidence of tuberculosis.

J. M. H. M.

ANIMAL AND VEGETABLE PARASITES.

TINEA OF NAILS WITH SUPERFICIAL GLABROUS RINGWORM OF HANDS AND FEET; TRICHOPHYTOID ERUPTION AFTER SPECIFIC INOCULATION. Seeman and Rajka. (*Arch. f. Derm. u. Syph.*, April, 1923, cxliii, section 1–2, p. 9.)

A woman, aged 27 years, who had had tinea unguium of both hands and the left foot for 7 years, was admitted with small, scaly, hyperæmic, circular, superficial lesions on both palms and their interdigital spaces. The left sole was less obviously affected.

Trichophyton gypseum was grown both from the nails and the eruption on maltose agar. Trichosan (Papay) was injected intracutaneously on June 21st. There was a positive reaction on the following day (negative in a control case). The pure culture was inoculated on scarified areas of the patient's forearms, and similarly in a case of latent syphilis as a control on July 4th. The latter reacted with marked local hyperæmia on July 6th, but there was no local reaction in the original case, who, on the other hand, showed erythema multiforme-like lesions on the dorsal aspects of hands and wrists (erythematous type of trichophytoid) as a result of the trichosan injection.

These lesions are to be regarded as an example of specific allergic reaction, and are thought to be due to "toxins" rather than the fungus itself, which could not be seen in or cultured from scrapings.

By July 10th *the control case* showed typical trichophytosis infection, from the purulent discharge of which the fungus was cultured and isolated. This did not occur in the original patient until July 18th, *i.e.* a very slow development, two weeks after the inoculation. It soon subsided spontaneously. The allergic eruption (trichophytoid) had completely involuted by July 19th, having lasted 12 days.

It follows from the experiments—

(1) That specific immunity exists in nail cases as well as in glabrous trichophytosis.

(2) Similarly, a trichophytoid eruption can be experimentally produced by intracutaneous injections of the trichosan (Papay).

(3) The palmar and plantar eruption, in which the fungus was easily demonstrated, clinically resembles so-called "summer exfoliation" of the palms.

H. C. S.

RINGWORM. Jas. Robertson. (*Brit. Med. Journ.*, June 16th, 1923, p. 1017.)

After cutting the hair short, washing the scalp with ether soap and drying, the author applies the following lotion: Calomel 5 gr. mixed in tinct. iodi one drachm. This, with the resulting red precipitate, is daubed on gently by means of cotton-wool, a dry dressing then being applied. The following day the head is washed with ether soap and then covered with ammoniated mercury ointment, the head then being again bandaged. This latter procedure is continued daily until cure is attained, the lotion being applied only the once. When the area of infection is very large the head is marked off into six divisions, and each of these is treated on successive days with the lotion. Too vigorous an application of the lotion results in a burn. Ringworm of the glabrous skin receives similar treatment. The author claims that in a series of sixty-one cases of school age the longest period required for cure was thirty-seven days.

M. S. T.

LEUKODERMA IN PITYRIASIS VERSICOLOR. Wertheim. (*Derm. Zeitschr.*, June, 1923, p. 343.)

If a case of pityriasis versicolor be exposed to the sun or to ultra-violet light, the normal skin reacts with erythema followed by pigmentation, while the diseased plaques stand out as yellowish, slightly scaling areas. In time, under

the influence of sunlight, the pityriasis clears up more or less completely, and the formerly diseased areas now appear of normal coloration, and stand out in striking contrast to the strongly pigmented surrounding skin, giving an appearance of leukoderma. A gradual disappearance of the fungus can be observed, which is practically complete eight weeks after an exposure to the "Hohensonne." A second exposure now results in an even pigmentation of the whole skin, showing that the leukoderma is due to absorption of the ultra-violet rays by the layer of fungus, and not to impairment of the pigment-forming function of the skin, as seems to be the case in the superficially similar syphilitic and seborrhoic leukodermas. J. F. S.

NEW GROWTHS.

EPITHELIOMA OF THE EYELIDS. D. W. Montgomery. (*Urol. and Cut. Review*, April, 1923.)

The author points out (1) the frequency of involvement of the lower lid as compared with the upper lid; (2) the marked resistance of the conjunctiva to invasion by an epithelioma on the skin surface or on the edge of the eyelid, and the freedom of the conjunctiva from the injurious effects of radium; (3) the excellent results from radium treatment. W. H. B.

GRANULOMA PEDICULATUM. Falkenstein. (*Derm. Zeitschr.*, January, 1923, p. 299.)

The author discusses the condition known as botryomycosis, granuloma pyogenicum and granuloma pediculatum. He gives a full histological description of a case which came under his notice, and concludes that the original lesion is of the nature of a capillary angioma. Three tumour-masses arising from a common pedicle were surrounded by the stretched and thinned papillary layer and unbroken epidermis. They consisted of numerous lumina, round, oval, or bottle-shaped, lined by plump, proliferating endothelial cells. Between these vessels were numerous cells indistinguishable morphologically and tinctorially from the endothelial cells, and, in fact, traceable to their origin in these. Elastic tissue was present abundantly in the thinned-out papillary layer, but absent in the tumour-masses. In spite of the unbroken epidermis there were present numerous masses of Gram-positive cocci throughout the specimen. He also gives a brief description of a more advanced lesion, showing how the picture of a granuloma becomes superimposed upon that of an angioma. J. F. S.

EPITHELIOMA ON LUPUS ERYTHEMATOSUS. Bagrow. (*Derm. Zeitschr.*, July, 1923, p. 83.)

A fatal case of epithelioma supervening on lupus erythematosus of seventeen years' standing. The patient had previously had X-ray treatment. The author could only find 32 cases of this in the literature. J. F. S.

PATHOLOGY.

THE RELATION OF ACNE TO VITAMINE STARVATION. A. Meska. (*Česká Dermatologie*, 1923, iv, p. 131.)

The author believes that acne depends upon vitamine B starvation of the

system. He bases his observations on the following facts: (1) Frequent improvement of acne by administration of vitamin B (yeasts, "Bicklein," regulation of diet). (2) Occurrence of acne in growing subjects, in the period of greatest need of vitamines. (3) Experiments on animals showing the relation between vitamine starvation, function of genital organs and skin disturbances. (4) Flaring up of acne in springtime following a period of lessened vitamine supply in winter food. (5) Favourite diet of acne patients usually is poor in vitamines (meat, fats, scanty vegetables). (6) Frequent dyspeptic troubles throughout the alimentary tract. SPINKA (St. Louis).

RONGALIT-WHITE STAINING IN SKIN-HISTOLOGY. PAKHEISER. (*Derm. Zeitschr.*, May, 1923, p. 263.)

THE author has employed rongalit-white for the demonstration of the nerves of the skin, following Kreibich and Frieboes. It appears that a much better picture is produced than by impregnation methods, inasmuch as the stain seems to be specific for the nerve-fibrils, whereas by the older methods it is often impossible to distinguish with certainty the nerves from the other fibrils which abound in the corium. The author in the main confirms the findings of Frieboes. J. F. S.

SYPHILIS.

THE SIGNIFICANCE OF THE LUETIN REACTION AS RELATED TO A BETTER DIAGNOSIS AND TREATMENT OF SYPHILIS. F. HERB. (*Urol. and Cut. Review*, March, 1923.)

THE author emphasises the importance of the luetin reaction in the later stages of syphilis and in congenital syphilis. If properly done he states that the reaction is specific and gives 100 per cent. positive results, whereas the Wassermann reaction is not uncommonly negative in asymptomatic syphilis.

"The luetin reaction is specific, and indicates that active spirochætes exist in the body." W. H. B.

SPONTANEOUSLY RELAPSING SALVARSAN ERUPTION. HARRY. (*Derm. Zeitschr.*, January, 1923, p. 305.)

THE author reports a case of this rare occurrence and quotes five others from the literature. His patient, a woman, aged 58 years, was infected at the end of 1919, and received in 1920 and 1921 three combined courses of neosalvarsan and Hg. In January, 1922, a fresh course was commenced. The first two injections were well borne, but a week after the third an erythematous rash appeared which became almost universal and was moist and weeping in the flexures. This lasted 74 days, and then for 23 days the skin remained well. Then, 97 days after the last salvarsan injection, a complete relapse occurred. This lasted for another 15 days, when the patient was dismissed cured, but with almost complete loss of hair. The author ascribes the cutaneous manifestations to injury of the vegetative nervous system. J. F. S.

THE INFLUENCE OF POTASSIUM IODIDE ON SYPHILIS, ESPECIALLY ON THE WASSERMANN REACTION. HIRSCH. (*Derm. Zeitschr.*, May, 1923, p. 273.)

HIRSCH records the results of intensive iodide treatment in 124 cases of late syphilis with positive Wassermann reaction, tabulated as follows:

46 cases of tertiary syphilis, 16 (34·7 per cent.) became negative.
26 „ early latent syphilis, 11 (47·8 per cent.) became negative.
34 „ late latent syphilis, 11 (52·9 per cent.) became negative.
14 „ latent syphilis, date unknown, 7 (50 per cent.) became negative.
7 „ parasyphilis, 6 (85·7 per cent.) became negative.

That is to say, of the 124 Wassermann-positive cases, 58, or 47 per cent., became Wassermann-negative. Thirty-four of these were re-investigated—after what interval is not stated—and 19 were found to have relapsed while 15 remained negative. There seemed to be no correlation between the amount of KI given and the effect on the Wassermann, as with total doses of 30–100 g., 48 per cent. of 52 cases became negative: 100–200 g. gave 56·1 per cent. negative out of 57 cases; while 200–300 g. gave only 1 success, or 11 per cent., out of 9 cases. J. F. S.

BISMUTH IN THE TREATMENT OF SYPHILIS. Joseph V. Klauder. (*Arch. of Derm. and Syph.*, 1923, vii, p. 721.)

This paper is a report on an experimental study of bismuth as a spirochæticidal drug in rabbit syphilis, and an account of the clinical results from its use in the treatment of fifty syphilitic human patients. The preparations employed were the French preparations of sodium and potassium tartrobismuthate in aqueous solution and in olive oil. The bismuth preparations were administered intramuscularly, as intravenous administration was contra-indicated, and were given in doses of 0·1 to 0·2 grm. every third or fourth day. Occasional untoward reactions occurred, such as foul breath, blue line on the gums, and stomatitis. Lesions of primary, secondary and tertiary syphilis were involuted after a total administration of 0·3 to 1·5 grm. of the bismuth preparation. The pain and local reaction following the injections was variable, the aqueous solution being more painful than the oil suspension.

Bismuth therapy is particularly useful in patients hyper-sensitive to arsphenamin. J. M. H. M.

BISMUTH IN THE TREATMENT OF SYPHILIS. J. G. Hopkins. (*Arch. of Derm. and Syph.*, 1923, vii, p. 745.)

The experiments here recorded show that in rabbits sodium and potassium tartrobismuthate are spirochæticidal and curative, and that a single injection of one or other of these preparations is as effective as neo-arsphenamin and more effective than mercuric salicylate. In early active human cases it would appear to accomplish at least a temporary cure, and its effect on latent cases suggests that it may be useful in the treatment of those which are resistant to other drugs. J. M. H. M.

BOOK RECEIVED.

Rhus Dermatitis: Its Pathology and Chemotherapy. By James B. McNair. 1923. Chicago: The University of Chicago Press. Price 20*s.* net.

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ERYTHEMATOID BENIGN EPITHELIOMA.*

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Under this heading I propose to group a series of cases which have occurred in my practice in the last four years, some of which have been shown at the Dermatological Section of the Royal Society of Medicine under other names. I hope to justify the title I have chosen, and to substantiate the claim that the group is really a new one, not previously co-ordinated or described. Several other cases than mine have been shown at the meetings of the Section after my first case was exhibited there, and all have followed more or less the pattern of that case. This paper is based on the study of seven cases. The essential features of the group may be briefly summed up as follows. There is an eruption of multiple (usually very numerous) slightly depressed, discoid, red patches, curiously like lupus erythematosus at a first hasty glance, and it is of interest that lupus erythematosus was the diagnosis universally offered for my first case until the histological sections had been inspected. This erythematoid aspect is so striking that I have not hesitated to put this character in the forefront of my title. Closer investigation, however, shows in the majority of cases at the edge of the red patch a very faint white-wax-like, shiny, sinuous, narrow raised margin, much flatter than the rolled edge of a rodent, but clearly of the same nature. However large may be the patch—and I have had a case which showed a patch $3\frac{1}{2}$ by $2\frac{1}{2}$ in. in area—the faintly raised waxy outline may usually be seen. Ordinarily the patches are much smaller, averaging in size a shilling, and in these the waxy outline is more easily discernible. In the very earliest

* Read at the Third Annual Meeting of the British Association of Dermatology and Syphilology in Liverpool, July, 1923.

stages the lesion is merely a white wax-like papule as big as a split-pea, but in a well-matured case these lesions may be entirely absent, and in any event the characteristic completed feature is the red discoid patch. Part of the patch may have undergone spontaneous involution and show a very superficial atrophy, again curiously resembling lupus erythematosus, and it is extremely likely that there are cases of this affection masquerading under the diagnosis of lupus erythematosus. In a few cases the patch may disappear, leaving a superficial scar; in the majority of cases the patch simply goes on extending by peripheral enlargement, the waxy edge being, as it were, pushed out, much as a wave of water, produced by throwing a pebble into a still pool, extends. True ulceration is as yet unrecorded, but there may be some small pustules, scabbed over, on the surface, or more exceptionally a velvety granulomatous growth, or possibly a keloid-like hard swelling may occupy a portion of the patch. I have seen all these forms in different patients. On palpating the skin of the patch between the finger and thumb the sensation is one of quite superficial infiltration, and that sensation is borne out by the microscopic sections, which show very superficial changes. The histology will be dealt with in detail later. Subjective sensations are almost entirely lacking in the patches, and in particular there is no gnawing pain so characteristic of rodent, though some itching and smarting have been mentioned by patients.

The *multiplicity* of the lesions is a very striking characteristic. In the first case, that shown by me at the Section in December, 1919, there were over a hundred distinct lesions, and this is certainly the largest number hitherto recorded. In this case one patch had developed a hard red, keloid-like growth, $1\frac{1}{2}$ in. long, $\frac{1}{2}$ in. wide, and about $\frac{1}{2}$ in. high, which showed typical rodent tissue on section. In two cases only were the lesions not multiple.

The *distribution* is very typical. The trunk is the site of election, the upper part of the chest and lower part of the back being perhaps the most favoured parts. In several cases the scalp, so rarely affected by rodent, was the seat of one or more lesions. The curiously extrafacial type of distribution, uncommon in rodent, is to be insisted on.

The *age of onset* is usually that of middle life—round about 40. The earliest age, that of the first case recorded, was 25.

Sex-incidence.—In the small list of cases which I have personally examined the preponderance of the female sex is remarkable, and

reverses the experience of rodent. Six out of the seven patients were women.

Benignity of type.—There was no glandular enlargement in connection with any of the lesions. Thus metastases were absent, and the benign character of the type, upon which the proposed title lays stress, is further evidenced by the duration of individual patches—in one of my cases 30 years, in another 21 years, with very little alteration other than a slow peripheral extension—and is supported by the absence of ulceration or local destruction other than a remarkably superficial atrophy. Pringle, commenting on my cases, mentioned a patient he had had who gave a history of fifty years' duration of one lesion. The benign character is further very remarkably emphasised by the undoubted spontaneous disappearance, without ulceration, of some lesions—a fact which was clearly demonstrated in several cases, both by the history and by finding flat discoid areas of atrophy, which had obviously been the site of previous active disease.

Differentiation of the Group from other Types of Epithelioma.

When the eruption of erythematoid discoid patches is well advanced, the appearances are so characteristic and so striking that confusion with other types of epithelioma can hardly occur, and it is indeed on the contrary difficult when confronted with one's first case to conceive of the lesions being epitheliomatous at all. Experienced observers have failed to recognise any similarity between these chronic red patches and any other variety of epithelioma, and the microscope has usually been the means of diagnosis. In several of the cases no lesions other than the red patches could be found, but the repeated history of patients that the red patches began as white pearly nodules leaves no doubt in my own mind that this beginning is the rule, and the pearly nodule is a factor common both to early rodent and to Brooke's disease. In this connection the combination of lesions found in the first case I showed, that of Mrs. H—, is especially instructive. Here there were very numerous pearly nodules, nearly as numerous erythematoid patches, and one quite characteristic hard large rodent tumour. The histological findings are equally instructive in this case. The pearly nodule showed an acinous arrangement of epithelial cells in the corium very like that found in Brooke's disease. The red patch, on the other hand—and the patient said that the patch had begun as a pearly nodule—showed very little if any deep epithelio-

matous invasion of the corium, and it would almost seem as if the red patch marked a phase of retrogression in the process of epitheliomatisation, and is in fact a step towards spontaneous cure—a view which is supported by the well-established observation that many of the red patches did in fact undergo spontaneous involution. The continuous enlargement of the majority of the patches does not entirely contradict this view, for the process may be active at the periphery while quiescent in the centre. However this may be, it seems justifiable to say that the development of the red patches is of good augury as compared with the progress of events in Brooke's disease and in Jacob's ulcer, in which the pearly nodule, the usual inception of both types, develops so differently. It is in fact in this phase of the completed erythematoid patch that the justification for making a separate clinical group of these cases lies, and it is just this erythematoid phase which has made their recognition as epithelioma so difficult and so delayed. But I am ready to admit, and indeed would emphasise my conviction, that all three types—Jacob's ulcer, Brooke's disease, and the group I am describing, are "sisters under their skin," and their differences are conditioned by the different manner in which the pearly papule, which is their common origin, develops. But these variations are so great that by common consent Brooke's disease has been clinically separated from rodent, and I submit that my group is equally deserving of separation both from Jacob's disease and from Brooke's disease. The salient features of distinction from Jacob's disease are, the multiplicity of lesions, the extra-facial distribution, their superficial position in the skin, which gives an appearance almost of depression of surface rather than of prominence, the absence of ulceration over periods of observation as long as fifty years, and the remarkable tendency to spontaneous involution. The preponderance of females, if borne out by wider experience, makes another note of distinction.

In the multiplicity of lesions, the comparative benignity and the relative absence of serious destruction of tissue, the type obviously resembles the rare and interesting group to which Brooke's name is usually attached, epithelioma adenoides cysticum. The appearance in early life of the lesions in the latter group, the familial history, the characteristically facial distribution, the much greater tendency to ulceration, and sometimes fatal ulceration, as I have seen happen twice, separate it readily from the type I am now proposing to create. The character of the individual lesions sets them poles apart. In Brooke's disease the typical development is the

fleshy salient nodule, with the rampart-like gristly wall round a pronounced depressed centre, a combination of appearances which allowed so experienced an observer as Allan Jamieson to mistake a case of Brooke's disease for molluscum contagiosum in a patient who retained this diagnosis for sixteen years, until it was ultimately upset only by a visit to the Section under my auspices. The histology of Brooke's disease is likewise totally different from that of the group I am attempting to make. In the latter, at any rate in the discoid patches, the epithelial downgrowths are typically shallow, contrasting strikingly with the deep-seated involuted pattern of downgrowths in Brooke's disease—a pattern which suggested Brooke's title of "adenoides." Clinically and histologically the types are so different as to lead to no possibility of mistake one for the other.

Much more difficult is the question of differentiation of the group known as Bowen's precancerous dermatosis, partly because that group is clinically so ill-defined that there seems to be little agreement as to what should or should not be included in that category. I have personally never seen a case that was definitely accepted as an instance of it, though many have been so reported, and some have been exhibited, without, however, commanding any wide assent to the diagnosis. Bowen, writing in 1915, counts six cases only as being recorded up to that date—three of his own and three described by Darier. These six cases, at any rate, collected and re-edited by Bowen, may be regarded as authoritative examples of Bowen's disease, and a perusal of their description is the most instructive preliminary to their distinction from the disease I am describing. I am, as I have admitted, handicapped by the fact that I have not seen personally a case of Bowen's disease, so that my knowledge of the clinical features is derived from reading only, but it would not seem very easy to confuse this type with "erythematoid benign epithelioma." In Bowen's disease prominent pale *red nodules* (not patches) were noted arranged in a roughly circinate or semi-circinate fashion, and the whole combination of lesion and shape of area occupied continually suggested to competent observers a tertiary syphilis—a diagnosis which would not occur to any dermatologist on seeing a case of the disease I am describing. The nodules are, in Bowen's description, very hyperkeratotic, often even papillomatous, tending to ooze and discharge, contrasting strongly with the flat and dry surface of my cases. It is expressly stated by Bowen that no spontaneous involution, so frequently mentioned in my description, occurred in any of his cases, and in the patients who could be followed

up malignant changes developed so frequently—in half of the cases according to Darier—that Bowen's title, *precancerous* dermatosis, is well justified. All these clinical features are unlike what my cases show. Histologically also the difference is notable. Both Bowen and Darier, and especially the latter, insist on a constant hyperplasia and œdema of the epidermis, and a marked dyskeratosis, evidenced by the presence of "corps ronds," "vacuolated cells," "clumps of nuclei in a clear space," etc., showings which I have not encountered in any of the sections I have examined from my cases.

Histological Characters.

Detailed notes of the histological findings in each case which I was able to examine will be supplied with the clinical record of the patients. In five of the seven I obtained the sections myself. In the sixth Dr. Gray examined the sections and reported the case as histologically a basal-celled epithelioma. In the seventh case a biopsy is unprocurable.

Differentiation must be clearly made of the type of lesion examined. The histology of the pearly nodule, found in some of the cases co-existing with the red patch, and stated in almost all cases to be the starting-point of the red patch, resembles closely the histology of the pearly nodule, which, as has been said, is the usual harbinger both of Jacob's disease and Brooke's disease, and the pattern of epithelial proliferation in the corium follows either the acinous arrangement of Brooke's disease (Mrs. H—'s case), or the arrangement of massed collections of epithelial cells, surrounded by well-developed fibrous envelopes, common in the various stages of Jacob's disease. Our interest lies rather in the histology of the completed erythematoid patch. The appearances shown are rather different according as one includes in the section the presumably advancing edge or the quiescent centre, and further, according to the degree of development of the edge, which in some cases was much more pronounced than in others. Thus in three of the patches (from Mrs. H—, Mrs. R—, Mrs. W—) the section apparently includes little of the edge, with correspondingly little of active disease. But inspection of these sections is very illuminating, for it suggests an involution of the progress of epithelial growth, if the patients' statements can be accepted that in the same site a pearly nodule had been noted earlier. In two other lesions (from Miss U— and Mrs. C. H—), clinically exactly similar, a much more

pronounced rodent type was present. The sections as a whole clearly establish the classification of the disease as a basal-celled epithelioma of rodent type, with (perhaps unusually) shallow invasions of the corium by epithelial downgrowths. I accepted this category in my earlier cases, and showed them as examples of "multiple flat rodent," but the clinical features are so unlike rodent that my first case shown under that title was derisively rejected, until sections were inspected, as belonging there at all, and the entire absence of ulceration over long periods of observation makes the diagnosis of "rodent *ulcer*" a contradiction in terms. On all these counts a new name for the group seems desirable, and I hope the name I have proposed stresses the salient characteristics and may thus merit adoption. I have chosen an English form for the title, as in that form the first word arrests attention to the most striking clinical character of the typical lesion, and its startling resemblance to lupus erythematosus. But it may be preferable to adopt Brooke's lead, that is, to Latinise the name and to call the group "epithelioma erythematoides benignum." I do not wish to perpetuate the term "rodent," which is, rightly, deprecated by continental writers, and prefer not to include that name in the title, but I wish it to be understood that the group is simply a species in that genus, and is, histologically, a basal celled epithelioma.

Association with Other Diseases.

There has been a curious frequency of a history of psoriasis in several cases reported. Gray's two cases had psoriasis. Pringle's case, if accepted as of this diagnosis, also had psoriasis. Mrs. Savill's case had a seborrhœid. Dr. Adamson, in the important discussion of cases reported in the Journal of July, 1922, suggests that some of the discoid patches might be mistaken for psoriasis, but the reports of this association have been made by competent dermatologists who would hardly make this mistake. The association is probably accidental, and there is no evidence of a patch of erythematoid epithelioma arising in the site of a patch of psoriasis. Both Gray and I have inquired into this minutely. In Gray's case, No. 3 of this series, there was a notable cancerous history in the family, but this does not seem to be common, or mentioned in the history of other cases. In Pringle's case, if accepted, the patches were preceded by an eruption of senile sebaceous warts.

Treatment.

Darier, in commenting on my three cases shown in March, 1922, considered X-rays the most desirable method of attack. Pringle, in the same discussion, gave as his experience in the case just quoted that both X-rays and radium had completely failed to improve any of the lesions, but freezing with carbon dioxide had succeeded much better. In my own case, No. 4 of this series, four applications of X-rays on the same patch over suitable intervals of time, and applied by so experienced a radiologist as Adamson, had produced no good effect. The same patch treated with freezing was practically cured. I have used this method in nearly all my cases, and consider it the method of selection. The applications I have made have been very light, with exposures of ten to fifteen seconds only, and I have had no contretemps with this treatment, even with so sensitive and delicate a woman as Mrs. W—, Case 4. As Dr. Whitfield pertinently remarked at the reading of my paper before the Dermatological Association, the experience that X-rays does not improve this type of epithelioma constitutes another reason for its clinical separation from Jacob's disease.

Case 1.—Mrs. H—, aged 46 years. This patient was shown at the Dermatological Section of the Royal Society of Medicine in December, 1919. She came to St. Mary's Hospital a week or two previously and showed a very remarkable eruption, the diagnosis of which remained uncertain in my mind, but I was disposed to accept it as a lupus erythematosus. There were three distinct types of lesion:

(1) A long keloid-like tumour on a red base and red throughout its consistence, situated just above the left clavicle, about 1½ in. long, ½ in. broad, and raised from the level of the skin by about ¾ in. She said that she had had this swelling for about eighteen months. There was no ulceration anywhere visible, either in the swelling or around it. My explanation of the swelling was that it might possibly be an epithelioma arising upon a patch of lupus erythematosus. This was excised forthwith and later examined histologically. There was no other lesion at all resembling this anywhere else on the body.

(2) Flat, red, discoid patches exceedingly like lupus erythematosus, the largest 1½ by 1 in. and averaging about ½ to ¾ in. in diameter. The surface was usually smooth, sometimes slightly mammillated, occasionally with small scabs occupying a portion of the red area, and still less frequently dotted with small lesions looking like drops of white wax upon the red base. In some of the patches, especially the larger ones, there was definite atrophy, and in most, but not quite all, of the patches, upon very careful scrutiny, a faint wax-like sinuous rim could be seen defining the red area, and creating an impression that the red part of the lesion was depressed below the level of the skin. There was no ulceration anywhere visible, the scabs being made up of epithelial cells matted together by serous or purulent discharge.

The discoid lesions of this type were exceedingly numerous, the largest occupying the space above the right scapula with another large lesion near the lower angle of the scapula.

(3) A third lesion, even more numerous than the red patches, consisted of a very faintly discernible white elevation, looking like drops of white wax splashed upon the skin.

The patient's description emphasised her conviction that all the patches had originated with the white lesions. She even gave a history that a white mark, possibly of this nature, had existed upon her chest since the age of about ten years, and that this had given rise to one of the red lesions. The next lesion to

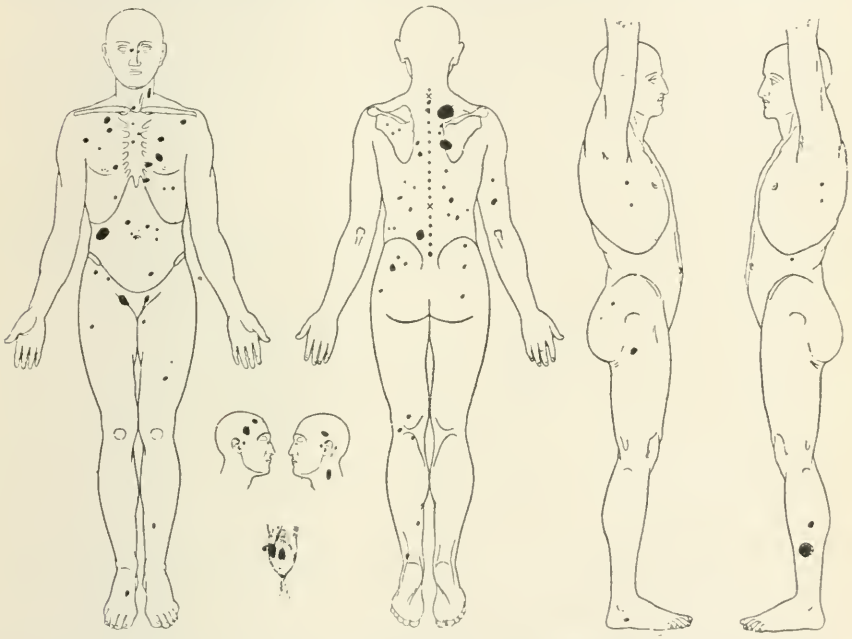

FIG. 1.—Case No. 1: Mrs. H—, *Brit. Journ. Derm. and Syph.*, February, 1920.

be noted was the largest one, upon the back, which had been observed at the age of twenty-five. The keloid-like mass she said had begun as a white papule about eighteen months previously, and had never gone through the red stage.

The lesions were counted and were well over one hundred in number, inclusive of the small white papules or nodules noted above. The distribution of at least the larger lesions is attempted in Fig. 1. There are scattered about the body several quite flat patches of atrophy, which the patient says were the site of previous reddened lesions which have disappeared spontaneously.

In other respects she is quite well and does a good day's work without difficulty.

This patient, as I have said, was shown at the Dermatological Section in December, 1919, and again in March, 1922. The sections shown at the first date clearly demonstrated the epitheliomatous character of the eruption, which had

not been suspected from the clinical aspect. It was recognised as being a type then quite new to our experience. At the next meeting of the Section another similar case (Miss U—) was brought up by Dr. Agnes Savill, who explained that having seen my case, the diagnosis, previously unsuspected by her, had become obvious. Dr. Savill was kind enough to allow me to see this case and make an ample note upon it, and to take sections, which I propose to show.

Case 1: *Microscopic notes.*—Three types of lesion were examined histologically.

(1) The large tumour on the neck.

Low power: The epidermis is thin. The whole of the substance of the tumour is made up of masses of epithelial cells, the masses being visibly derived from the basal layer and not particularly from any appendage of the skin.

Higher power: The stratum corneum is almost represented by a single layer. The stratum granulosum is present two or three cell layers thick. Prickle-cells in the rete have their prickles intact. There is no dyskeratosis, no vacuolation, no round bodies of Darier. There is no inter-cellular œdema. In the cell masses in the corium the prickle-cells have been lost to a great extent.

(2) Pearly nodule.

A fragment was taken from one of the pearly nodules.

Low power: The epidermis is thin throughout the section. The whole corium is filled with small round masses of epithelial cells rather resembling adenoid formation. This section is more like the appearance of Brooke's disease than any other section examined.

Higher power: On examination with the higher power the stratum corneum was very deficient. Prickles were completely present throughout the rete There was no intercellular œdema and no dyskeratosis of any kind. The masses of cells in the corium, while much smaller in extent than in the section just described, are of exactly the same nature.

(3) A fragment of skin was taken from a reddened patch. The section bears out the clinical characters very remarkably.

Low power: The epidermis is everywhere thinned at the edge of the section, which corresponds with the margin of the patch. A very superficial down-growth of epithelial cells is found, derived apparently from the basal layer and not in any connection with the hair-follicle or the sebaceous gland. There are no deep collections of cells as in the other two sections.

Higher power: A certain degree of cicatricial atrophy may be assumed from the appearance of the rest of the section, vessels being few and the skin appendages little marked.

Case 2.—Florence U—, aged 43 years, a single woman. Shown by Dr. Savill at the Royal Society of Medicine, January 15th, 1920; described, *British Journal of Dermatology and Syphilis*, April, 1920. The Section immediately accepted this case as being of the same character as my first case. Two types of lesion were again notable here: (1) A discoid red patch exactly like the lesions in Mrs. H—'s case, the largest being found just below the angle of the right scapula, $1\frac{3}{4}$ by $\frac{3}{4}$ in. in area. This lesion was oblong, but the others were more commonly discoid. The surface was of a bright red, quite flat, with some small wax-like nodules studded over some patches. In one of these patches, $\frac{5}{8}$ by $\frac{1}{4}$ in. in area, complete involution had taken place in the centre, leaving an atrophic scar surrounded by shiny papules, the combination closely resembling lichen planus annularis. The lesions were slightly itchy or tingling—a sensation

something between a burn and an itch—and sometimes shooting pain was felt in them. They tend to bleed when rubbed. In several instances spontaneous involution of older lesions had taken place.

(2) Small white shiny nodular lesions, in some cases appearing to be made up of white follicular papules forming a small plateau-like elevation, many of them not exceeding $\frac{1}{8}$ in. in diameter. The patient says that all the lesions began in this way.

She has not had any general eruption on her body before, but in the last few weeks has developed an eruption, almost certainly a seborrhœid, on the chest, arms and back, in fact from the neck to the ankles, but not upon the face, quite distinct, very itchy, and not in any way connected by her with the old eruption.

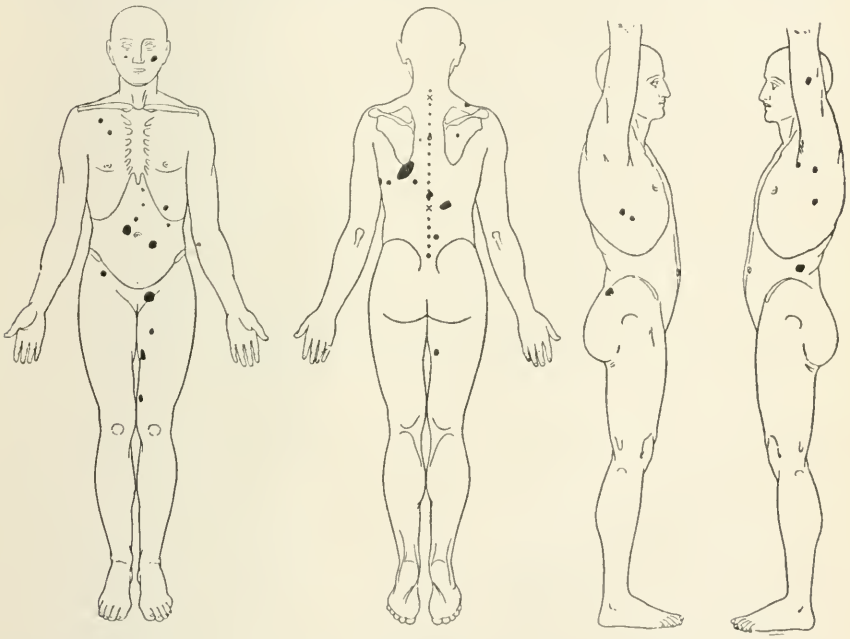

Fig. 2.—Case No. 2: Florence U—, *Brit. Journ. Derm. and Syph.*, April, 1920.

There is no history of cancer in this patient's family. One maternal uncle died of consumption of the bowels at the age of thirty.

This patient also seems to be in quite a fair state of general health.

My warm thanks are due to Dr. Savill for her generous gift of this case.

Case 2: *Microscopic notes.—Low power*: The epidermis is very thin on most parts of the section. Immediately below the epidermis, and connected with it in some cases by an isthmus of epithelial cells, large masses of epithelial cells of the rodent type may be seen.

Higher power: Stratum corneum is a few lines thick. Stratum granulosum normally present in the greater part of the section. There is no vacuolation or dyskeratosis. No œdema of epidermis or corium. The cells in the massed collections in the corium are of the same type as those described above.

Case 3.—The patient is a man, aged 52 years, named H—, under Dr. A. M. H. Gray's care, and is the third case of the disease exhibited at the Royal Society of Medicine. Date of showing, February 19th, 1920; report, *British Journal of Dermatology and Syphilis*, July, 1920, p. 233. Dr. Gray obtained sections of this case, which reveal a typical basal-celled type of epithelioma. This patient showed lesions of the discoid red type exclusively. The first lesion began on the left cheek twelve years ago. Three years ago it was treated with radium by Dr. Lynham at the Radium Institute under the direction of Dr. Stowers, who was then acting for Dr. Gray; a scar remains *in situ*. He has one large lesion on the back of the trunk on the left side of the vertebral column at about the level of the twelfth dorsal.

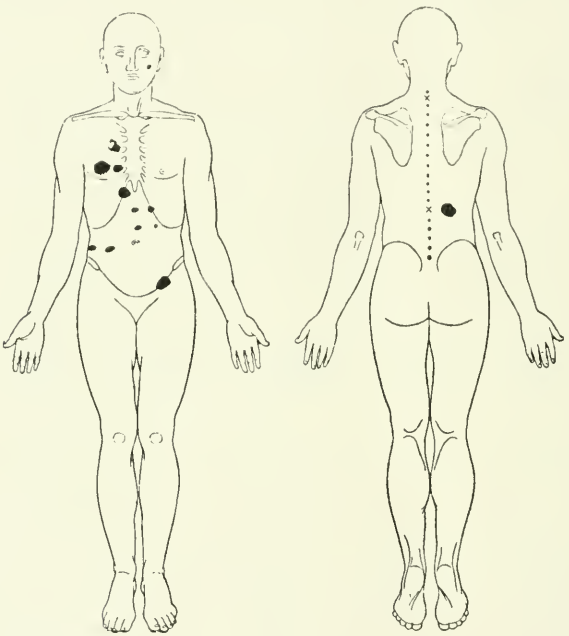

Fig. 3.—Case No. 3: Mr. H—, Dr. Gray's case, *Brit. Journ. Derm. and Syph.*, 1920, p. 233.

All the other lesions, about eleven in number, are distributed on the front of the trunk in the positions shown in Fig. 3; their circinate character is very well marked. They vary in size from $\frac{1}{2}$ in. to $1\frac{1}{2}$ in. in area. All the lesions are flat and red. There is very little sign of the waxy narrow margin, but this can be made out in some of the smaller lesions. There are no examples of the pearly nodules, as noted in the previous two cases. There is no ulceration in any of the patches. In some of the patches, and very notably in the large patch above the right breast at the level of the third rib, there has been a partial spontaneous involution, leaving a depressed white scar.

This patient has suffered from psoriasis since the age of 15 years, and there are numerous typical patches of psoriasis on the elbows and the trunk at the present time. They are quite characteristic patches of psoriasis and are

absolutely distinct from the epitheliomatous areas. No epithelioma seems to have developed on any previous psoriatic site. The man is otherwise in fairly good health.

He gives a remarkable history of family cancer. One brother had rodent of the eyelid, two uncles had cancerous growths cut out from lip and neck. His first wife died of cancer of the liver seven years ago; they had lived together for fifteen years.

Case 4.—Mrs. W—, aged 54 years, a private patient, came to see me shortly after I had shown my first case. She was a very frail and delicate woman, extremely thin. The lesions are all of the red discoid type, and the description given of the red patches in Mrs. H—'s case applies perfectly to these. The first

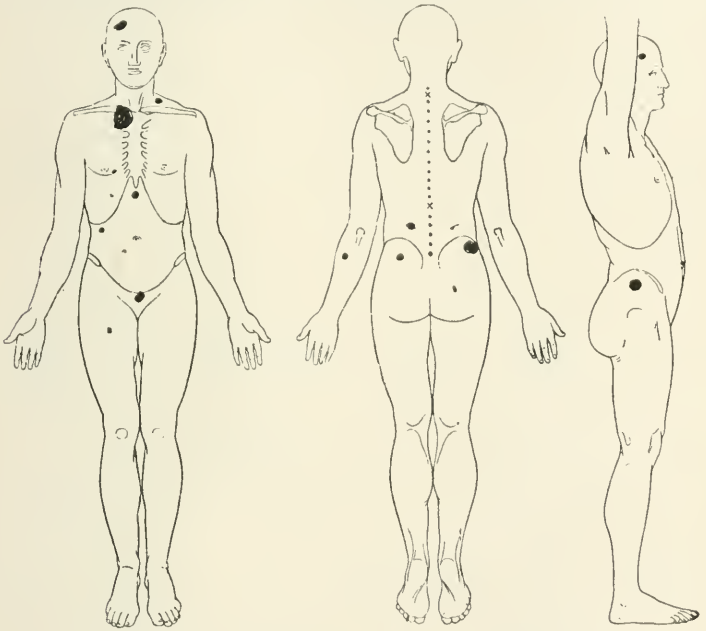

Fig. 4.—Case No. 4: Mrs. W—, private patient.

lesion to be noted was over the right clavicle some nine years ago. The second lesion appeared on the upper abdomen. The other lesions came out almost simultaneously and are now eight in all. The largest patch, and the earliest, lies just over and below the right clavicle. It is 3½ by 2½ in. in area, and shows several small cicatricial patches in which apparently spontaneous involution has taken place. Encircling the reddened area almost continuously is a very well-defined waxy raised edge, the edge in some places being exaggerated into small nodules of the same translucent waxy type, and in close proximity to the large and old area there are numbers of waxy nodules, some of them joining up with the rolled edge circumscribing the patch. The lesion upon the upper abdomen is slightly scabbed in parts and shows some purulent discharge at one edge.

She was seen by Dr. Adamson five years ago and was X-rayed four times

altogether on one patch, but without any improvement of it. Dr. Adamson was kind enough to look up the notes of this case after I showed it at the Section, and allowed me to read what he had then written. His diagnosis had been a very tentative one of lichen planus, to which later he had added equally tentative ones of "rodent" and "lupus erythematosus." The distribution in this case is indicated in Fig. 4. It will be noted that she had one lesion upon the scalp. She complains of a pricking sensation in some of the patches.

I have since treated the large patch with carbon dioxide freezing and have produced a nearly complete cicatrisation and blanching of the old area by this means.

Case 4: Microscopic notes.—This case shows a remarkably superficial epitheliomatosis, but in my opinion a true one, although this is disputed by the pathologist of my hospital. Dr. Adamson, to whom I have shown the section, supports my view that it represents a very early rodent type, and in this case one of the downgrowths of epithelium seems to start at the side of a well-developed pilo-sebaceous follicle. There are no deep collections of epithelial cells in the corium.

Case 5.—Miss C—, aged 72 years, was brought to me a few days ago by Dr. Gayner, of Redhill, to whom my thanks are due for the very careful diagram

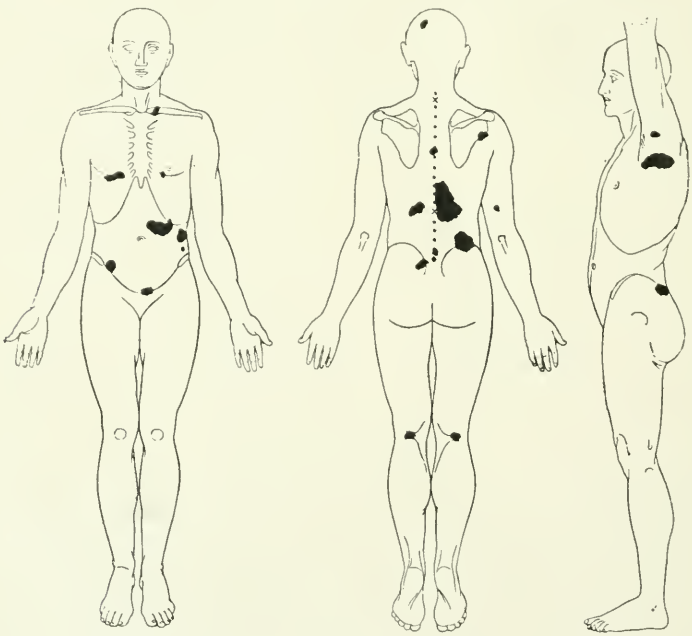

Fig. 5.—Case No. 5: Miss C—, private patient.

appended (Fig. 5). The lesions in her case are all of the reddened discoid type, the largest and oldest being found on the back, and here one patch has existed for over thirty years. I was not able to make a very complete examination of this lady as she refused to show me more than a very restricted part of the body,

and it was with great difficulty that her friend and general practitioner was able to persuade her to let him see the rest. She also shows a well-defined lesion upon the scalp, and this area, about the size of a shilling, is entirely devoid of hair. The patch exhibited to me, that just above the right breast, shows a very complete and characteristic translucent wax-like rolled edge. No ulceration has taken place in any of the patches, but on the large patch on the back there is a mass of warty granulation-tissue, which Dr. Gayner has from time to time reduced with local treatment.

Considering her years this lady is in very good general health.

No biopsy was obtainable.

Case 6.—Mrs. R—, aged 72 years, first came to see me at St. Mary's Hospital on July 11th, 1921. Shown Dermatological Section, March 15th, 1922; report,

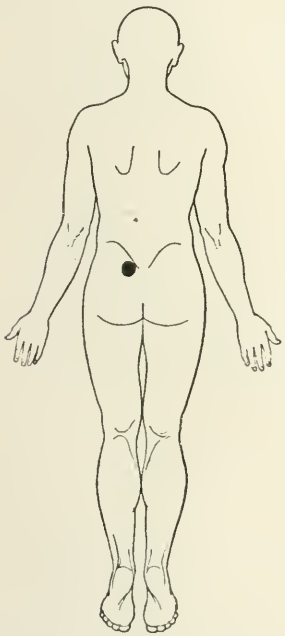

Fig. 6.—Case No. 6: Mrs. R—, *Brit. Journ. Derm. and Syph.*, July, 1922.

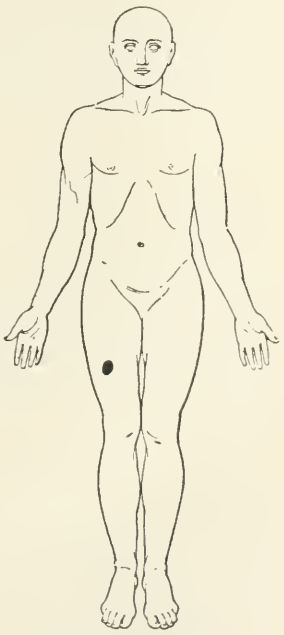

Fig. 7.—Case No. 7: Mrs. C. H—, *Brit. Journ. Derm. and Syph.*, July, 1922.

British Journal of Dermatology and Syphilis, July, 1922, p. 246. She showed on the lower part of the back just above the eminence on the left buttock a single circinate patch, red all over its surface, quite dry and smooth, and showing a sinuous faint waxy edge. The patch was of the size of a two-shilling piece, and is said by the patient to have come ten years ago in the site of a scratched mole which had been present all her life. There are no other lesions anywhere on the body.

I have treated this patch with carbon dioxide snow, which seems to have removed the diseased area completely.

Case 6: *Microscopic notes.*—In this case there is very little change in the skin. There are a number of shallow downgrowths over a certain area of the section, but there are no cell masses separated from the epidermis in the corium. It is remarkable that this case, though histologically somewhat indefinite, was clinically a perfectly clear example of this affection and so accepted by the Section.

Case 7.—Mrs. C. H—, aged 37 years, was brought to see me by Dr. Bennett, of Billinghurst, February 6th, 1922. Shown Royal Society of Medicine, March 15th, 1922; report, *British Journal of Dermatology and Syphilis*, July, 1922. She showed a single discoid red patch the size of a two-shilling piece, with a very narrow wax-like rolled edge surrounding it. She gave a history of this area having slowly developed within the last ten years. There are no subjective sensations complained of in connection with this lesion. There is no history either of phthisis or cancer. A small fragment of the patch was sent to me for examination by the courtesy of Dr. Bennett, to whom my best thanks are due.

Case 7: *Microscopic notes.*—This case, clinically exactly like the case just described, shows quite definite rodent type cell collections filling the corium.

References to Earlier Cases.

The only reference which I have come across to an observation which antedates my first case is in a monograph by Fordyce on "The Pathology of Malignant Epithelial Growths of the Skin" (*Journ. Amer. Med. Assoc.*, November 5th, 1910, lv, pp. 1624–1638), and I propose to end my paper with a transcript of a paragraph which is curiously anticipatory of much that I have written here.

Extract from Fordyce's Monograph.

"Many multiple epitheliomata in the early stages closely resemble Paget's disease. They present all grades, from pale and red scaling patches the size of a split-pea or smaller to patches as large as the hand. They have sharply defined, scalloped margins, showing very slight tendency to elevate or pearly rolled edge. Some of them maintain their red and scaling appearance and others become the sites of fungating growths (Fig. 16). These tumours often develop on patches of seborrhœic dermatitis, which suggests some infectious agent. It is possible that the bottle bacillus, in combination with the staphylococcus, stimulates epithelial proliferation. Even in the early stages, before any apparent thickening of the epidermis is present, proliferation of the basal layer can be determined by histologic examination."

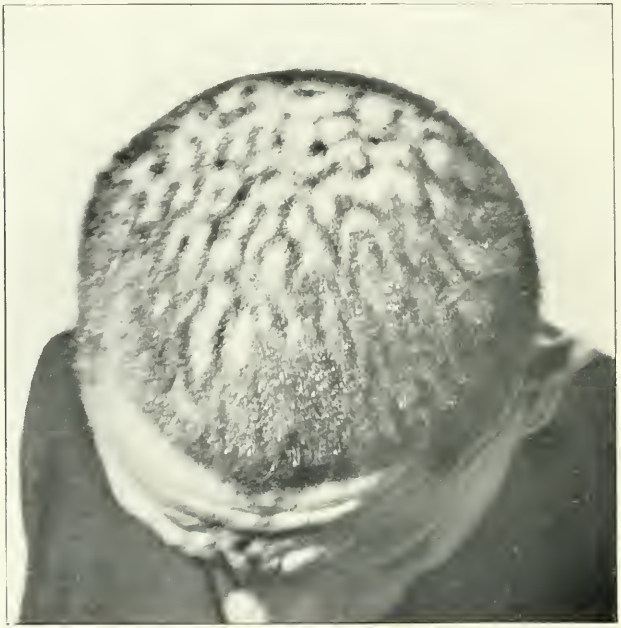

FIG. 1.

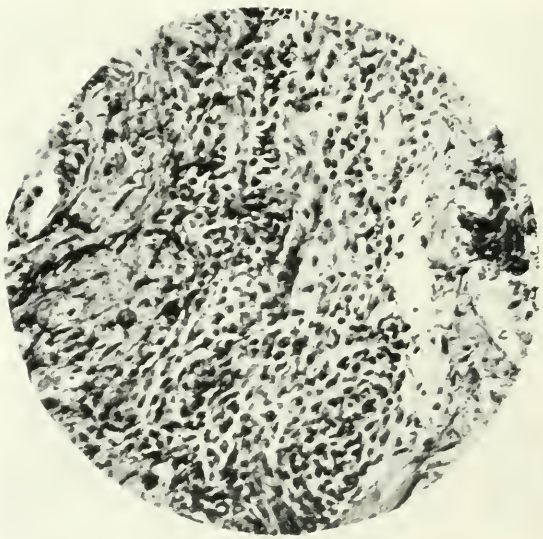

FIG. 2.—Section showing groups of cells with large nuclei, closely packed together, with a suggestion of a "whorl" arrangement.

TO ILLUSTRATE DR. M. G. HANNAY'S ARTICLE ON CUTIS VERTICIS GYRATA.

CUTIS VERTICIS GYRATA.*

M. G. HANNAY, M.D., M.R.C.P.,
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Report of case.—The subject is a male Jew, aged 24 years, short, dark, thick-set, but not obese. He was born in England, of healthy Polish parents, and has one brother who shows no abnormality. His own general health has been good, but he has suffered from some skin trouble nearly all his life. As quite a young child he was subject to eczema of the scalp. In later years, though the scalp remained free, he developed a more or less generalised dry pruriginous eruption, which at different periods assumed the appearance of prurigo, eczema, or diffuse pruritus with lichenification. There still remains some slight thickening of the skin of the neck and arms. In spite of the fact that he was almost constantly under observation at one or other of the London skin departments, the condition of the scalp was only noticed last year after a rather close hair-cut.

The condition of cutis verticis gyrata is present over the vertex and occiput. The surface is normal, and there are no subjective symptoms. The blood-count, both total and differential, is normal. The Wassermann reaction is negative, and other systems are normal.

The appearance is well seen in the accompanying photograph (Fig. 1), and corresponds exactly with the descriptions and illustrations of the majority of the examples of this anomaly which have previously been published.

Histology.—The epidermis shows no change. Through the whole of the corium, but especially around the follicles, are scattered irregular areas of slight cell infiltration of an inflammatory nature. In some sections, especially near the bottom of a sulcus, in addition to the slight inflammatory reaction there are deep-seated groups of cells with large nuclei, closely packed together (see Fig. 2), and in places almost having a regular linear arrangement. There is no excess of pigment. The appearance of the sebaceous glands, sweat-glands and elastic tissue is normal.

* The case was shown at the Section of Dermatology of the Royal Society of Medicine on March 15th, 1923.

Between thirty and forty examples of this anomaly are to be found in the available literature, but it is probably less rare than this limited number would suggest. V. Veress was able to collect 11 personal cases, and mention is made from time to time of others which have apparently not been published.

The first case was shown by Jadassohn at the Ninth Congress of German Dermatologists in 1906, when he also described two others. The next year Unna reported 3 cases, and introduced the name of cutis verticis gyrata. Audry published the first French example in 1909, under the name of pachydermie occipitale vorticellée. Important contributions followed by v. Veress (11 cases), Vignolo-Lutati, Malartic and Opin, Wise and Levin (the first American case), Lenormant, Alderson and others.

Most authors since 1914 have recognised two types, and a short separate description will perhaps help to emphasise the points of difference.

The great majority of cases, including the one reported above, belong to the first type. This usually appears after the age of 20. (Of 34 cases, 1 dated from birth, 2 from childhood, 4 from the second decade, and the remainder were not discovered until after 20 years of age.) All the subjects were males, usually with coarse dark hair. The area affected shows prominences, separated by furrows, which are occasionally straight, but more often irregular. The maximum change is nearly always in the mid-line, over the vertex, or occipital region, extending symmetrically in all directions, until merging imperceptibly with the normal skin. When different regions (*e. g.* the forehead in Stuhmer's case) or multiple areas (three in v. Veress' fourth case) are affected, the symmetry still remains absolute.

The scalp is generally lax, but may be firm. The surface appears normal. The hairs are bunched together in the furrows, and spread out as they emerge at different angles from the convexity of the folds, giving the appearance of a relative alopecia. There are no subjective symptoms. (Vignolo-Lutati's and Wise and Levin's cases complained of tenderness, and were possible exceptions.)

The various theories and pathological findings have been recently fully reviewed, especially by Lenormant, but as no previous case has been discussed in this country, a brief *résumé* may be given.

Jadassohn thought the condition might be regarded as an anomaly of congenital development, belonging to the large class of nævi. Unna

suggested a disproportion between the skull and the scalp—an atrophy of the one, or an enlargement of the other; if it were to be classed as a nævus, it must be of the type which appears late in life. V. Veress found in one case disappearance of sebaceous glands, atrophy of sweat-glands, and diffuse cellular infiltration of the corium, the changes predominating at the site of the furrows. But in another case none of these changes were present except a slight degree of atrophy of the sebaceous glands. He considered the condition developed subsequent to a chronic inflammation starting in the furrows. Vignolo-Lutati agreed with v. Veress as to the inflammatory origin, but thought the process started in the prominent portion of the folds, where he found deep-seated inflammatory infiltration with a tendency to sclerosis. In Hudelo and Richon's case there was folliculitis and perifolliculitis, with atrophy of sebaceous glands and disappearance of sweat-glands.

In support of the inflammatory origin, it has been pointed out that many cases suffered in childhood from eczema of the scalp, but in the majority the condition under consideration has not been noticed until after the age of 20, and no case has been immediately associated with clinical manifestations of inflammation. The histological findings in my own case tend to support the view of the nævoid origin, the inflammatory changes being secondary.

The second type, represented by the cases of Malartic and Opin, Lenormant, and Alderson's first case, is characterised by a definite tumour formation, with raised abrupt margins. The gyri are more numerous, and the sulci deeper.

The symmetry was not perfect in Lenormant's case, and the affection was on the right side in Malartic and Opin's patient. All the cases were in females, and all dated from birth, though considerable growth occurred in later years. Itching, discomfort and fœtid discharge were present in the cases of Malartic and Opin, and Lenormant. Alderson's patient complained of attacks of headache and nausea, but this may have been due to other causes. All cases required operation.

Malartic and Opin found increased pigment, and masses of nævoid cells. They regarded their case as a giant nævus of the scalp. Civatte, in summing up the microscopical appearances in Lenormant's case, says: ". . . ces éléments caractéristiques de la tumeur (*sic*) sont évidemment des cellules nœviques." Alderson found dense collections of pigment in the upper corium, and large cords or whorls of "connective

tissue " in the deeper layers, and looked upon the condition as a congenital connective tissue growth involving the skin.

At the time of writing this note, Fischer's article in the *Archiv für Dermatologie und Syphilis*, 1922, was not available. According to an abstract by Ch. Audry in the *Annales de Dermatologie et de Syphilis*, October, 1923, Fischer describes another case of the " mollusciform nævus " type.

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(19) Hudelo et Richon.—*Bull. de la Soc. Fr. de Derm. et de Syph.*, 1923, xxx, p. 311.

AN HITHERTO UNDESCRIBED FAMILIAL DISEASE.

M. SYDNEY THOMSON, M.A., M.D., M.R.C.P.,
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To claim any manifestation as being new in the experience of man would be deemed an impertinence by many philosophers. Two patients who have recently attended King's College Hospital would seem to warrant such an assertion however, at least in regard to this country. Search for any description which might tally with their clinical condition has proved unavailing, whilst they are thought to be unique by more than one experienced dermatologist.

Family History.

The mother, who was married in 1910, is now 31 years of age. Her father died of pulmonary tuberculosis, and apart from this fact there is nothing of note in her family history, whilst she herself has always been healthy since suffering from the usual acute specific fevers during childhood. There have been six pregnancies only :

No. 1.—A male child born in 1911. He died of " convulsions " at the age of eleven months. The mother states that this child had a rash on the buttocks which started at 8 months and persisted until death. The eruption occurred on the buttocks only and never showed any scaling, and is said to have been " very similar " to the condition to be described in Nos. 5 and 6.

No. 2.—A boy born in 1912, who died on the 8th day, probably owing to the fact that he was an 8 months baby.

No. 3.—This girl was born in 1914. At the age of $3\frac{1}{2}$ years she suffered from measles, which was followed by an acute mastoiditis on the right side. Since then 6 operations have been necessary, and even now she has to attend hospital daily for dressings.

No. 4.—A boy born in 1919. Apparently absolutely healthy.

No. 5.—This girl was born in 1921 and is Case A.

No. 6.—A female child born in June, 1923. This girl is Case B.

No miscarriages have taken place, whilst the only worries during pregnancy have occurred whilst carrying the last two children. The mother then had to take No. 3 to hospital for dressings, etc. She thus had both physical and mental strain during the last pregnancies.

The father was a prisoner of war, and on repatriation in December, 1919, he was pensioned for psychasthenia. No other noteworthy facts were discovered, either in his family history or in his own past history.

The Wassermann reactions of the whole family are negative.

History of Case A.—This child was carried during the abnormally hot summer of 1921, and was born normally at full term. She was breast-fed for 8 months. Walking occurred at the age of 15 months; the first distinct words were heard seven months earlier. No illnesses have beset her, and she "seems normal in every way except for a rather bad temper." No abnormal signs have been found in the chest and abdomen other than the presence of early rickets, as evidenced by tibial softening, beading of the costo-chondral junction, nocturnal restlessness and marked head-sweating. This diagnosis is further supported by the fact that "she seems much better in herself" since taking cod-liver oil and malt for the last three months. She has always been rather undersized.

There is a history of occasional nasal discharge, but Mr. Hope has on two occasions found only slight adenoid hypertrophy. There is absolutely no evidence of sepsis.

History of Case B.—The child was born at full term, the birth being normal except for the fact that it was slow and extended over three days. She is still being breast-fed and is puny and small. There is a vague and rather unsatisfactory history of maternal impression during the third month of pregnancy.

The heart, lungs and abdomen appear to be normal, but there are very definite bony deformities.

The membrane bones of the skull appear large in proportion to the cartilage bones of the face, imparting an indefinite Mongol appearance to the child. The disproportion is probably due to under-development of the latter as the cranial vault measurements are normal.

The metacarpals and phalanges of both hallnces are completely absent, whilst both ulnæ and radii are rudimentary, the latter particularly so.

This child also has suffered from occasional rhinorrhœa, but no marked abnormality has been found. There is slight adenoid thickening, and the tonsils are small and buried. The result is only a slight deficiency in the nasal airway.

Clinical condition of Case A.—The condition was first noticed at the age of 1 month, when a small red patch of the size of a threepenny-piece

FIG. 1.—Showing the condition on the face of Case A.

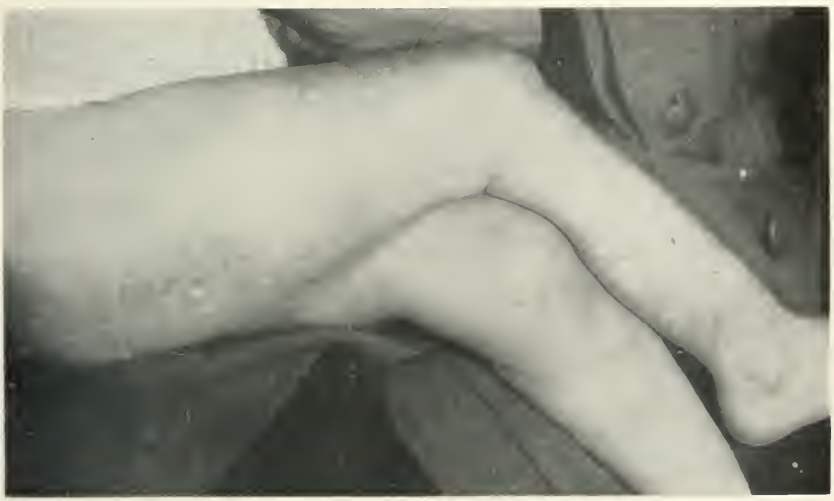


FIG. 2.—The distribution on the right thigh and leg of Case A.

TO ILLUSTRATE DR. M. SYDNEY THOMSON'S ARTICLE ON A HITHERTO UNDESCRIBED FAMILIAL DISEASE.

was seen on the most prominent part of each buttock. It next appeared on the face, and since then has gradually but constantly spread.

When first brought to King's College Hospital the striking appearance presented by the face was almost startling. Both cheeks were slightly swollen, tense and highly polished. Their colour was bright vermilion. In the centre of the affected area on the right cheek was an almost circular white patch. Pressure resulted in the disappearance of the colour to a great extent and revealed a certain amount of underlying telangiectasis. The whole of both buttocks showed exactly the same changes. The hands were cyanosed and swollen, whilst the feet were unaffected.

The child was treated with small doses of thyroid only, since when the general condition of the girl has considerably improved and the cyanosis has departed. The tense swelling of the face and buttocks has disappeared, whilst the intensity of colour in the affected areas has decreased. But the nævoid condition became more marked and appeared on the dorsum of the hands, extending a short way up the forearm. Here, however, it rapidly died down somewhat and left a very mild degree of pigmentation. A similar state of affairs existed on the feet and ankles.

Such was the condition in May last when this case was shown before the Dermatological Section of the Royal Society of Medicine by Dr. Arthur Whitfield.

To-day the distribution of the eruption is still more extensive. The whole of both cheeks are affected, whilst early changes are appearing on both eyebrows and at the free edges of both ears. Both arms from 2 inches above the elbow right down to the finger-tips show the same condition, but on the dorsal and external aspects only. Extension over the whole of both gluteal regions and thence down the thigh to the ankle has occurred, but again only posterior and external surfaces are affected. The knees, however, are wrapped round by the rash as by a bandage, the only areas in the whole body where the internal aspects show changes. The feet now show changes over a small part of the dorsum only. These are the only regions in which disappearance of the condition has taken place, for in May even the toes bore these same nævoid telangiectases. This event would seem to support the prophecy of ultimate disappearance made by Dr. Whitfield at that time.

The whole of the trunk is still absolutely clear.

As now seen, the condition may be said to resemble erythema *ab igne* most closely in regard to the general impression caused by its appearance.

It calls to mind, too, an exaggeration of the normal marbling of the skin. The nævoid condition seems to have resolved itself into a dilatation of the capillaries which take part in the presentation of these two better-known entities. The network seems rather more close however, so that some new formation may possibly have taken place. But this point is not really very clear, although some support is given by the fact that the holes of the net are in places larger than normal, as is seen in the large white patch on the right cheek. These larger areas always have been clear and do not appear to have changed in size or in configuration at all. They are not scars, and no scarring is anywhere apparent.

Pressure results in complete fading at the edges of the eruption, whilst in the centre a faint pigmentation is left as though some trace of blood-pigment has escaped into the tissues along the lines of the capillaries, for the network appearance is still maintained, blood returning along the same strands on release of the pressure.

The tensity which was at first present has now completely disappeared, and palpation demonstrates no trace of infiltration although the skin feels a little harsh over the affected areas.

Close examination of the surface shows it to be slightly shiny and very finely wrinkled. The wrinkling does not closely resemble that seen where the epidermis is œdematous, nor does it seem to be exactly like that seen in senile skin. It seems rather to partake of the qualities of both.

There has been present since birth the faint capillary nævus of the occipital region, and it is noteworthy that this has not changed in appearance or in size.

No subjective symptoms have ever been present, although the mother states that the child " feels the cold very much " ; the rash then becomes blue, and at these times is most reminiscent of the " marbling " in normal skin. The opposite occurs in sunlight or in front of the fire, when a brighter red appears.

But local excitation is not the only cause of increased intensity of colour, for the mother is positive that " it always looks much redder when the child is teething." Indeed this was the first statement she volunteered when asked if the rash ever changed colour. She has always used Knight's velvet skin soap, and this has apparently never produced any irritation.

Clinical condition of Case B.—In this patient the eruption first made its

appearance when the child was 3½ months old. It differed from the first case in that the face was first affected and then the buttocks, each of the four distinct areas spreading rapidly.

As in her sister a tense pink swelling was first seen, this being only very slightly raised above the level of the surrounding skin. Gradually the capillary network has become more obvious, appearing through the pink haze rather as the picture appears during the developing of a negative.

At present both cheeks and both buttocks bear areas of the size of a florin. Recently a distinct white patch of the size of a large pea has emerged on the left cheek. There is also a patch on the extensor surface of each forearm.

These latest areas are of importance as they are the earliest lesions that have been examined, in that they were seen within 48 hours of their first appearance. Over the centre of each area there were tiny papules which closer examination revealed to be solely follicular. There was no trace of hyperkeratosis and the condition seemed to be due to erection of the follicles owing to some excitation. Thirty-four days later these had resolved themselves into minute hyperkeratoses, which have since almost entirely vanished and left no trace. These papules were completely restricted to the centre of each patch. The mother states that she has always noted a "nutmeg-grater feel" over each area as it first appeared.

The general picture now presented exactly corresponds to that seen in Case A.

But there is in this patient one other fact which is of importance. In the centre of the forehead there is a pale capillary nævus of the type commonly seen in this situation. It was present at birth and has never changed in any way whatsoever.

Histology.

A piece of skin was removed from the outer side of the right leg of Case A at the end of September.

The horny layer is undoubtedly thickened, but it is compact and shows no sign of parakeratosis. The granular layer is very well developed and is also more pronounced than normal, but in places it varies in thickness. The stratum mucosum is in its greater part nearly normal, although it also varies in thickness in a few places, following the stratum granulosum. There is a slight widening of the intercellular channels with consequent

stretching of the intercellular fibrils. In one or two places it is considerably reduced in thickness. The stratum cylindricum shows deviation from the normal in many places, where it is compressed and stretched; even neighbouring cells are broken away from one another in these areas. But there is no sign of acantholysis, the process apparently being merely one of mechanical rupture. Occasional pigment-cells are interposed among the basal cells and the superimposed spinous cells. There does not seem to be any true mole formation, although this picture would seem to resemble such a process. There is one further point in that mitosis is not limited to the basal cylindrical layer.

The epithelial ridge and papillary processes are lost, whilst the junction of the epidermis and pars papillaris is frequently indistinct.

In the corium there is marked irregularity of the fibrous tissue of the pars papillaris. It is œdematous and contains blocks of a hyaline material which is most probably coagulated plasma, as the capillaries are distinctly dilated. There are a fair number of oval pigment-cells, and also some with definite processes. The pigment appears to be melanin, as it does not react to the tests for organic iron. There is a distinct increase in the number of small round-cells and fibroblasts. The pars reticularis shows little deviation from the normal, but the vessels seem to be somewhat distended. They are not obviously greater in number than normal, and there are no signs of angiomatous changes. The sweat-glands show definite dilatation, and in one or two places the epithelium is separated with the resulting formation of a double cyst, which is quite obviously not the cross-section of a branching coil.

In brief then, there is hyperkeratosis with slight œdema, irregular acanthosis and mechanical disturbance of the epidermis. In places there is some atrophy. There is loss of papillæ, confusion of the epidermodermic boundary and hyperpigmentation. There is a cellular infiltration of the pars papillaris and marked œdematous congestion. There is a cystic dilatation of the sweat-glands.

Discussion.

These cases are apparently unique, and can be said to raise suggestions of erythœdema and angioma serpiginosum as the only possible differential diagnoses.

The clinical appearances are obviously quite different from either. The cases cannot even be accounted as anomalous instances of the "pink

disease" for many reasons. There is no suggestion of "raw beef hands and feet"; the distribution of the changes is more extensive, and these make their first appearance on the face and buttocks. The swelling is here only transitory. But the most important facts are the complete absence of irritation and total lack of the marked systemic phenomena so obvious in erythrœdema.

Angioma serpiginosum shows grouped vascular points, whilst these cases show no suggestion of the "grains of cayenne pepper." There is no central clearing as the lesion spreads peripherally. No fresh points develop immediately beyond the affected area, for this is essentially a "creeping eruption." Also it is difficult to imagine angioma serpiginosum starting in so many widely separated spots more or less simultaneously. Lastly, the histological appearances completely controvert the possibility of angioma.

Whilst it is impossible to indicate the cause of the changes there are one or two points worthy of note. In the first place the condition definitely makes its appearance on what might be termed the traumatic areas of childhood, to wit the cheeks and buttocks. As the child grows it spreads to the outer aspects of the legs and the dorsum of the forearms —regions more liable to injury than are other parts of the body.

The suggestion conveyed by the clinical appearances is most obviously that of an exaggeration of the normal capillary network of the skin—an impression which is apparently confirmed by the histological pictures of the vessels. They dilate on exposure to heat or sunlight whilst contraction and cyanosis occur on exposure to cold.

These points, together with the œdema and slight infiltration of the skin, would seem to indicate a reaction to external irritation—an abnormal reaction certainly, in that the exciting cause must be very slight, whilst

the reaction is apparently wholly that of slight changes consequent on capillary dilatation. The important factor would therefore appear to be the abnormal excitability of these vessels, possibly through their nerve supplies, as follicular excitation is an early accompaniment of the first appearance of the condition. Dilatation of the sweat-glands is also present, and although mechanical obstruction resulting from the hyperkeratosis may be the cause of this phenomenon, it is possible that it may be due to hypersecretion.

Mention of the sympathetic nervous system provides a strong temptation to continue along these lines, but after all they are only vague hypotheses, and it would undoubtedly be more discreet to draw to a speedy conclusion.

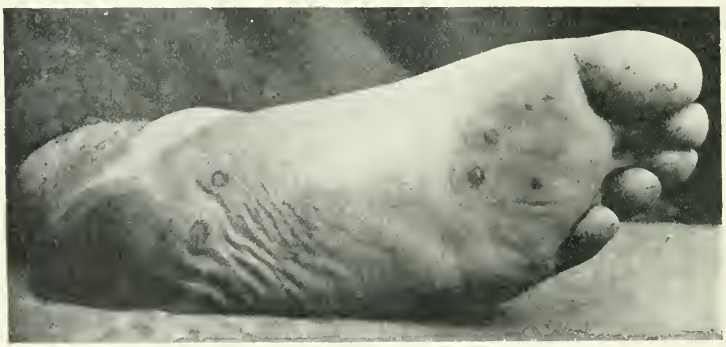
To Dr. Whitfield my earnest thanks are due, both for permission to publish these cases, and for considerable help in the elucidation of the histological appearances.

CLINICAL NOTE.

A MILD CASE OF KERATODERMIA BLENNORRHAGICA.

P. B. MUMFORD, M.B.Vict., M.R.C.P.Lond.,
Assistant Medical Officer, Manchester and Salford Skin Hospital.

Although several examples of this disease have been recently described, it was thought that the following case might be of interest on account of the short duration and mild nature of the skin manifestations.



The type here described is probably not as uncommon as dermato-

logical literature would lead one to suppose—partly because the period of the existence of the lesions is so brief, and partly because the discomfort to which they give rise is overwhelmed by the other symptoms to which a generalised gonococcal infection usually gives rise.

Two distinct types of the disease are described, one in which the lesions are general, and one in which they are confined to the hands and feet—an excellent example of the former, which had a fatal termination, was described in a recent number of this Journal by Gibson.

The patient, a healthy adult male of 22 years, noticed a urethral discharge on July 28th. Three days later he attended a public clinic with a severe pustular urethritis. He was found to have a Gram-negative intracellular diplococcus in the discharge.

On August 4th he complained of pain in the left testicle and pain on defæcation; on the following day inflammation occurred in the right ankle-joint. On August 8th the arthritis spread to the left shoulder, left knee- and ankle-joints. He then was compelled to go to bed owing to the severe pain, malaise, headache and loss of appetite; there was a definite evening temperature.

On the last-mentioned date he noticed what he describes as a "soft scabbed wart" on the dorsum of the first interphalangeal joint of the left big toe; a similar "wart" was present on the right big toe. These were followed within a few days by about a dozen similar warts on the soles of both feet. The remainder of the body remained unaffected except for a lesion which appeared under the right ear. He states that the lesions were painful to the touch at first, had a thin scab, and did not bleed easily.

On examination on August 12th the lesions were flat, moist looking papillomatous lesions; two were scabbed over. They were flatter and less filiform than the so-called "gonorrhœal wart" frequently seen in cases of chronic urethritis and vaginitis, where it is confined to the areas directly irritated by the pustular discharge.

The lesions were not confined to pressure points on the sole, and one small group was clustered over the left big toe; they were slightly painful when pressed, appeared to be superficial and free from deeper tissue; a faint zone of inflammation was present around each.

Histological examination was not permitted.

A detoxicated gonococcal vaccine (5000 million) was given, and one week later he returned with the lesions looking flatter and with less

discharge. An ointment of 5 per cent. salicylic acid cleared away the remnants in a few days, leaving faint brown pigmented areas.

The joint condition has slowly progressed, and at the date of writing the ankle alone remains painful.

OBITUARY.

Dr. WALLACE BEATTY.

Dermatology has suffered a real loss in the death of Dr. Wallace Beatty, which occurred on November 8th. For some years he was on the Editorial Staff of this Journal, and made several interesting and valuable contributions.

He was also an active member for over thirty years of the Dublin Biological Club, to which he brought forward many dermatological cases, some of rarity, illustrated by beautiful histological slides.

Dr. Beatty had troops of friends and was esteemed and loved by all who knew him, for the tendrils of affection cling more closely to nobility of character than to special accomplishments.

He was a man of transparent honesty and goodness of heart, ever unmindful of self, and generous in his estimation of others.

The writer of this article was his intimate friend for fifty years, and never knew any man who was so rich in that charity which "thinketh no evil."

He had a hyperæsthetic conscience, and was unselfishly liberal to his poorer patients, even to his own detriment.

From his brilliant student days to the close of his active life his motto was—"Whatsoever thy hand findeth to do, do it with thy might."

In addition to the crippling infirmity of increasing deafness, he bravely bore a long and trying illness with the calm cheerfulness and courage the fruit of a blameless life.

The Board of Trinity College, Dublin, recognised his worth a few years ago by creating for him the post of Hon. Professor of Dermatology, a distinction which he highly appreciated.

Walter G. Smith.

DR. WALLACE BEATTY.

CURRENT LITERATURE.

INFLAMMATIONS, ETC.

NOTE ON "BAKER'S ECZEMA." TANKARD. (*Lancet*, August 11th, 1923, p. 279.)

THE author calls attention to eczema on the arms of bakers caused by potassium persulphate added as an "improver" to the flour. This salt, $K_2S_2O_8$, when it comes in contact with water produces potassium acid sulphate, $KHSO_4$. Investigation showed that the suspected flour contained this chemical to an appreciable extent, although the amount was not sufficient to cause any noticeable increase of the normal content of mineral matter in flour of that grade. A flour may appear normal in every respect and yet contain persulphates for which a specific search must be made.

The cases of eczema to which the author refers were only found among workers who used flour containing persulphates, and then only when the flour was handled in a moistened state; when this flour was not used, but flour free from persulphates substituted—with salt, yeast, etc., as usual—no trouble was experienced, and the eczematous condition of the skin of the affected workers gradually disappeared. J. A. D.

THE ÆTIOLOGY OE KALA-AZAR AND TROPICAL SORE. BLACKLOCK. (*Lancet*, August 11th, 1923, p. 273.)

THE theory which associated kala-azar with the bed-bug has not yielded definite results, and that which has connected it with various flagellates infesting plant bugs has been negatived by the assumption that these bugs do not bite man. The author draws attention to the fact that at any rate one species of plant-bug —the *Dysdercus superstitiosus*—does bite man, and cites instances in which he himself was bitten twice accidentally and once experimentally by this insect. The occurrence of flagellates in plant-bugs has been emphasised by other writers, and evidence is available of the ability of these flagellates to infect the alimentary canal and salivary glands of the bugs. If therefore it is found that bugs which usually live on plant-juice and which are capable of harbouring flagellates in their salivary glands are able to bite man, it is a strong argument for further investigation in this direction, especially as it has been stated that the parasite of tropical sore will grow on a medium containing certain plant-juices.

J. A. D.

THE OBJECTIONS TO THE CONCEPTION OF THE LICHENIFICATIONS. L. BROCQ. (*Ann. de Derm. et de Syph.*, May, 1923, VIe série, tome iv, No. 5, p. 273.)

IN this article Brocq contests with his usual skill the views put forward by Dind in the *Annales*, 1920, p. 283. Briefly stated, Dind's thesis was that the "lichen simplex chronicus" of Vidal or the "névrodermite circonscrite et diffuse" of Brocq and Jacquet and lichen planus are in reality one and the same affection, and should be classed together simply as "lichen"; moreover he endeavoured to establish that "lichen," both in the form of lichen simplex and of lichen planus, is a chronic *infectious* disease, the infecting organism being at

present unknown. Those who have read Dind's original article will hardly need Brocq's arguments to convince them of the futility of attempting to prove that lichen planus and lichen simplex are the same condition; that any dermatologist of experience should hold such a view is hardly conceivable. Nevertheless Brocq's article is well worth reading, as it is a model of incisive reasoning.

H. W. B.

AMYLOIDOSIS OF THE SKIN. Juliusberg. (*Derm. Zeitschr.*, August, 1923, p. 153.)

The author describes anew a case reported by him in 1900, and at that time undiagnosed. It presented numerous firm papules on both legs, of a dull bluish-red colour, and showed microscopically a change in the white fibres of the corium which gave the staining reactions of amyloid. In the light of the article by Gutmann (*Derm. Zeitschr.*, April, 1923, p. 65) he now considers the case one of multiple localised amyloidosis of the skin. His case suffered also from true prurigo of Hebra, Gutmann's from acrodermatitis atrophicans. J. F. S.

PINK DISEASE—ERYTHRŒDEMA. E. Sydney Littlejohn. (*Med. Journ. of Australia*, June 23rd, 1923, p. 689.)

Dr. Littlejohn believes that "pink disease" is an infectious disease of the nervous system, analogous to infantile paralysis and lethargic encephalitis, and involving especially the vaso-motor centres in the medulla and spinal cord. Like these diseases, it occurs sporadically and in epidemics. Unlike them, however, it is absolutely confined to infants and young children. The site of entry of the infection is in all probability the naso-pharynx.

The disease is a clinical entity and conforms to type. When the symptoms are well advanced the condition is quite characteristic. The child is generally crying and whining, with an expression of the most utter misery. It seems to dread being touched or disturbed. In bed it either sits with its head bent forward right down between its knees, or gets on its hands and knees and buries its face in the pillow. Photophobia is a very frequent symptom; it appears early and generally persists for some weeks. The child is extremely fretful, rubs and scratches its body and limbs and picks at its fingers and toes. Sweating in many instances is very profuse, and the hands and feet are of a peculiar pink colour and are cold and clammy. The pinkness does not as a rule extend above the wrists and ankles. It is always symmetrical and is generally an early symptom, appearing in two or three weeks from the onset, though its appearance is sometimes delayed for four or five months. It is pathognomonic. Often the tip of the nose, the cheeks and the ears are pink. Wasting and muscular weakness are early symptoms. Complete loss of appetite is constant, as also is insomnia.

The profuse sweating often causes an extremely irritable miliarial rash with vesication and desquamation. In some patients deep ulceration of the palms, soles and buttocks and loss of finger- and toe-nails may occur. Some degree of stomatitis is of frequent occurrence.

American writers state that the disease is constantly preceded by a naso-pharyngitis, and that the naso-pharynx is probably the site of inoculation of the disease. The deep reflexes are always diminished and sometimes absent, and cutaneous sensibility to pinprick is sometimes lost.

The symptoms persist for at least several weeks and often months. Improvement is shown by cessation of fretfulness and sweating, return of appetite, sleep and muscular power. The last sign to disappear was always the pinkness of the hands and feet.

Recovery is complete: there is no record of any sequela, and no instance of a recurrence.

The mortality is probably about 4 or 5 per cent.

The occurrence of the disease in epidemic and sporadic form, its self-limitation, its seasonal incidence, the presence of fever and the leucocytosis all suggest strongly an infection. Treatment has hitherto been symptomatic, but Vipond* reports that he treated two patients with a vaccine prepared from a diplococcus discovered in the lymphatic glands. The reaction was slight, and in three days both patients showed a definite improvement. After a third dose one patient was practically cured. J. H. S.

QUININE MELANOSIS IN A CASE OF PEMPHIGUS VULGARIS.

FUNFACK. (*Arch. f. Derm. u. Syph.*, August, 1923, cxliv, Part II, p. 194.)

THE production of melanosis by quinine is exceedingly rare. In this case of pemphigus the drug had been administered both intravenously and *per os*, with some benefit to the patient (a married woman, aged 53 years), for about a month (45 grm. quin. *per os*, and 5 grm. intravenously), when pigmentation was manifested in the healthy skin and buccal mucous membrane, hitherto unaffected by the disease. The bronzing was slight at first but gradually increased, and after 15 grm. more of the drug had been given in 10 days, reached a degree comparable to that of the negro, with additionally blue-black pigmentation of the buccal mucosa. There was neither melanuria nor alteration in colour of the fæces, and the usual symptoms of quinine intolerance remained entirely absent throughout. On remission of the drug the melanosis slowly cleared up. The mechanism of production of pigmentation generally, and the two main types of animal pigment, *i.e.* hæmatogenous and autochthonous, the latter of which contains no iron, are discussed at some length by the author. He also touches upon the hypothetical relationships of the adrenal body, the sympathetic nervous system and the skin, and introduces some possible hypotheses to explain an indirect action of quinine in this particular case. In his final conclusions, however, he prefers to believe that the drug acts directly on local function in the pigment cell-layer, and is therein comparable to the much-studied action of arsenic, which, as is well known, can always be demonstrated locally in such cases. H. S.

KERATOSIS GONORRHOICA PROVOKED LOCALLY BY X-RAYS.

OELZE. (*Arch. f. Derm. u. Syph.*, June, 1923, cxliv, Part I, p. 1.)

THE interest in this case lies in the accidental sensitisation of the skin of the knee-joint by X-rays (half the erythema dose through 3 mm. of aluminium), and the appearance after a latent interval of four days of typical lesions of keratodermia blenorrhagica in a very unusual situation. It should be noted that the patient had been admitted with active gonorrhœa, synovitis of the left knee-joint and the rare but typical dermatosis on the feet. The X-rays had been given with

* Vipond, A. E., *Archives of Pediatrics*, November, 1922.

a view to relieving the pain of the synovial effusion. In view of their recent origin it was hoped that these lesions would contain gonococci, which have never yet been isolated from this dermatosis. All microscopic and cultural investigations failed, however, to demonstrate them. The article is well illustrated by actual photographs. H. S.

GONORRHŒAL KERATODERMA. Arthur W. Stillians and Erwin P. Zeisler. (*Arch. of Derm. and Syph.*, 1923, viii, p. 393.)

A case of gonorrhœal keratoderma with generalised lesions in a man, aged 29 years, is here reported. The case is well illustrated, and the histological detail carefully described. The writer considers that the keratotic exanthem is peculiar to the gonococcal infection, and quite distinct from arthropathic psoriasis, to which the lesions bear a superficial resemblance, but their conical shape and waxy translucency enable them to be distinguished from ordinary psoriasis. J. M. H. M.

TREATMENT OF URTICARIA WITH COLLOSOL MANGANESE. H. McCormick Mitchell. (*Brit. Med. Journ.*, 1923, ii, p. 563.)

Four chronic cases of obscure origin are discussed in detail. Intra-muscular injections were given at weekly intervals, starting with a dose of 0·5 c.c. and increasing to 2 c.c. A minimum of four and a maximum of seven injections were necessary to produce freedom from symptoms. The longest period of observation since treatment is fourteen months. M. S. T.

AUTO-HÆMOTHERAPY BY CUPPING IN FURUNCULOSIS AND CARBUNCLE. J. Billaux. (*Journ. des Sc. Méd. de Lille*, 1923, xli, p. 409.)

A case of rapidly extending carbuncle is reported which had been treated surgically by means of the thermo-cautery on the fourth day of the disease. On the fifth day the condition was worse. The cautery was again used, and also dry-cupping was applied over the dorsal and lumbar regions. Eight hours after this there was very marked local and general improvement. Cuppings were repeated for several days, and again later, when a few small boils appeared round the margin of the lesion. Recovery was complete in a month. Quotations are given from other authors dealing with the principles involved.
M. G. H.

DERMATO-MYOSITIS. F. G. Finley. (*Canad. Med. Assoc. Journ.*, June, 1923.)

Of this rare condition the author records a case occurring in a soldier during the war. The diagnosis was suggested by the tender, brawny, spindle-shaped swellings on the forearms, and somewhat similar ones on legs, accompanied with considerable functional disability. Confirmation of the diagnosis was confirmed by post-mortem—the patient dying shortly after admission to hospital. The marked degenerative muscle-changes are described, and micro-photographs shown. The cutaneous manifestations were not present in the case recorded—but when present they usually simulate erythema nodosum. The ætiology of this disease is still wrapped in mystery. W. H. B.

PURPURA HÆMORRHAGICA AND APLASTIC ANÆMIA DUE TO CHRONIC BENZOL POISONING IN A CANNING PLANT. H. B. Anderson, J. S. Boyd and A. B. Jackson. (*Canad. Med. Assoc. Journ.*, June, 1923.)

The increasing use of benzol and its congeners for industrial purposes makes this publication of interest to dermatologists, and more especially from the scientific standpoint, on account of the light thrown upon the ætiology and pathogenesis of purpura hæmorrhagica from a study of the toxic effects of benzol. The three cases recorded occurred in a factory for manufacturing sanitary tin cans. The sealing medium, which consisted of gum rubber, beeswax and an inert colouring matter dissolved in benzol was the source of trouble. The sealing solution was applied mechanically and the benzol driven off by heat. The plant had been in existence for nine years, and no previous trouble had been known. One case, a young girl, who had only been employed three months, died within a week after coming under observation with all the signs of an acute purpura hæmorrhagica. Another case, an adult male, had had epistaxis coming and going for six months prior to observation, but got well under treatment and removal from his work. The third case, an adult female, also showed acute symptoms after three months in the factory, and died shortly after coming under observation.

Since these cases occurred, the various steps taken to prevent further trouble are described. W. H. B.

CHALASODERMIA OR "LOOSE SKIN" AND ITS RELATIONSHIP TO SUBCUTANEOUS FIBROUS OR CUTANEOUS NODULES. F. Parkes Weber. (*Urol. and Cut. Review*, July, 1923.)

Of this very rare condition the author describes three main types: (*a*) A true elastic skin, due to excess of elastic tissue, with imperfect attachment of the skin by fibrous trabeculæ to the deeper structures. (*b*) Another type where there seems to be a deficiency in true cutaneous elasticity, but with hyperplasia of the white connective-tissue elements; as a consequence the skin tends to become "baggy" over parts of the body. (*c*) A third type where the skin becomes loose and abnormally movable owing to a deficiency of the fibrous trabeculæ. The author records cases associated with multiple fibrous or calcareous nodules. A very full list of references is given of all the recorded cases, and a brief mention of the relationship of cases of "loose skin" to trophœdema and Milroy's disease. W. H. B.

IMITATION CONEY SEAL-SKIN FUR DERMATOSIS. R. Prosser White. (*Urol. and Cut. Review*, July, 1923.)

In the recent outbreak of fur dermatitis in England the principal culprit was found to be "coney seal," which is the cheapest and most common variety of fur-edging on the market. In the curing, tipping and finishing of natural skins skin troubles arise mainly among the workers, but in the making of cheap substitutes mordants and dyes have to be employed, so that the wearers as well as the workmen suffer.

The author in this article gives an interesting and detailed account of the various processes of curing, killing, mordanting and dyeing the furs, and the *raison d'être* for dermatitis. In the dyeing process residues are often left in

the furs in the cheaper processes, but in high-class careful dyeing they are cleared out by frequent washings. "Brush-dyeing" is one of the most persistent causes of trouble. Prevention of trouble can only be attained by extreme care being taken in all the different processes, particularly to the final washing of the fur. W. H. B.

SYPHILIS AND ULCUS MOLLE.

THE INTRAVENOUS USE OF COLLOIDAL MERCURIAL PREPARATIONS IN SYPHILIS. Teichmann. (*Derm. Zeitschr.*, July, 1923, p. 25.)

A colloidal calomel preparation seemed to have fewer disagreeable effects than ordinary preparations, but to be correspondingly feebler. A preparation containing in addition calcium or strontium in order to minimise the vasomotor effects was still under trial, but so far had proved ineffective. The first preparation is to be used in conjunction with salvarsan, and alone only if the latter is contra-indicated. J. F. S.

SALVARSAN-RASH AND LICHEN RUBER. Riecke. (*Derm. Zeitschr.*, July, 1923, p. 1.)

Now and then in cases of salvarsan-rash there occur mucous-membrane lesions of identical origin but of varying clinical appearance. The exanthem, too, may occasionally resemble a well-defined dermatosis, as pityriasis rosea, or lichen planus. He records in detail a case in which there developed after a course of silber-salvarsan a rash which resembled in places lichen planus, in others lichen acuminatus, and in others seborrhœic eczema. The histological picture of lesions excised from the back and from the mucosa of the cheek he considers to exclude true lichen planus. Two cases are given for contrast in which true lichen planus developed during a salvarsan "cure." Only by their histology can "circumscribed salvarsan-rash" be distinguished certainly from lichen planus. J. F. S.

THE SEDIMENTATION OF THE BLOOD IN SKIN AND VENEREAL DISEASES. Kersting. (*Derm. Zeitschr.*, July, 1923, p. 33.)

Glass cylinders are filled with 2·5 c.c. of 1·1 per cent. citrate of soda, and 7·5 c.c. of blood obtained by venepuncture, and well rotated to ensure thorough mixing. The height of the column of clear plasma in millimetres is read at intervals. Normal readings after one hour are—men 3–5 mm., women 5–8 mm.; after two hours, 6–10 mm. and 8–13 mm. respectively. The room-temperature has a marked effect on the readings. The results are tabulated in 140 cases, of which 78 were syphilis. In syphilis a marked acceleration of sedimentation goes roughly with a positive Wassermann reaction. Wassermann-negative cases, treated or untreated, give normal or only slightly raised rates. Eczema gives variable results, but generally speaking, the more acute and the wider spread the eruption, the higher the reading. Psoriasis, even when generalised, gives normal readings. Experimentally, high readings could be induced in normal subjects by provoking a severe erythema on the back with the "Hohensonne." This reaction has little or no practical value in diagnosis. It seems to depend on agglutination of the red cells. J. F. S.

MAXIMAL EARLY TREATMENT OF SYPHILIS. Hoffmann and Hofmann. (*Derm. Zeitschr.*, August, 1923, p. 129.)

In spite of all the advances in the treatment of syphilis, there is a constant tendency to increase the antiluetic pharmacopœia. Bismuth seems destined to replace mercury, which it excels in spirochæticidal power, and is to be used in combination with arsenicals. The authors consider that not enough emphasis is laid nowadays on the outstanding property of salvarsan, its power of curing absolutely an early infection, whether acquired or congenital. They hold that the so-called abortive treatment should not be reserved solely for the early sero-negative case, but should be extended also to all primary and early secondary cases. They have seen permanent cures of such sero-positive cases even after moderate courses, and consider that more intensive treatment would increase the number of such. A further argument for the intensive "cure" is that many patients when once freed from symptoms fail to return for the later courses of the "intermittent" system. Their first dose is 0·45 neosalvarsan for a man, 0·3 for a woman, and further doses of 0·6 or 0·45 are given every 4 or 5 days, or even twice a week, until a total of 5·5 or 6·5 gm. has been given. A second course is given 5–6 weeks later, while the Wassermann reaction is still negative from the first course. Should the Wassermann reaction become positive before or during the second course, a third course is given (Sicherheitskur). Congenital cases should be treated if possible *ante partum*, but even after birth the above principles are considered applicable. J. F. S.

ALTERATIONS OF THE CEREBROSPINAL FLUID IN NON-NERVOUS CASES OF SYPHILIS, AND THEIR PROGNOSTIC SIGNIFICANCE. M. Pappenheim. (*Arch. f. Derm. u. Syph.*, June, 1923, cxliv, Part I, p. 117.)

In his conclusions the author believes increased C.S.F. pressure to be premonitory rather than actual evidence of meningeal involvement. Increase in the cell count may occur in sero-negative cases, and before even adenitis can be demonstrated. A similar precocity is noted in some cases for the gold-sol and hæmoglobin reactions. Globulin is a later manifestation, and occurs as a rule only after the adenitis becomes evident. As soon as the Wassermann reaction becomes positive in the blood, the pathological findings in the C.S.F. increase both in number and degree, and reach their maxima in the tenth month after infection.

Thereafter the percentage of positive findings decreases, until in the tertiary stages of latency they reach a proportion of 20 per cent. of all cases examined, and of these only about one-half show serious pathological changes. Subjective nervous symptoms occur for the most part in C.S.F. + cases, but may also occur with the liquor apparently healthy.

At present nothing definite with regard to cutaneous eruptions and liquor changes in relation to them has been proved, but it seems pretty certain that luetic alopecia and a positive C.S.F. finding are in constant association.

The frequency of positive C.S.F. results in later and tertiary syphilis finds no agreement among the authorities. Of great importance, if correct, is the statement that antispecific treatment in the secondary period must be regarded as *provocative* in effect, if only of ephemeral duration. Stress is laid on intensive treatment as of great value, in the early stages of C.S.F. involvement, and

perhaps of benefit within the first two years of infection. Regarding prognosis, this author is of opinion that increased pressure and globulin content are not by themselves of serious import, but that syphilitics in the latent tertiary stages with pronounced changes in their C.S.F. are in considerable danger of metaluetic (tabes, G.P.I., etc.), complication at some future date. The converse is, however, also true and well known to neurologists, viz.: because a patient has a negative C.S.F., it by no means follows that he is safe from the later nervous manifestations of the disease. (This would seem to argue the independence of meninges and white or grey matter of the cord, etc., from each other, and the possibility of infection of one or other separately and apart from each other.) From these undoubted facts the indications for treatment receive no direct support, and we are still advised to base our therapeutic endeavours on the requirements of the individual case. H. S.

INVESTIGATION OF SPIROCHÆTA PALLIDA FROM CULTURES. HOFMAN. (*Arch. f. Derm. u. Syph.*, August, 1923, cxliv, Part II, p. 306.)

THIS studious and patient inquiry, the practical object of which it is not easy to discern, occupies over 50 pages of the text, and also cites 4½ pages of bibliography. In his first, of three parts, the author emphasises the variations in tissue and cultured spirochætes, and also the differences in length, breadth, turns of the spirals, etc., according to the nature of the culture medium, whether solid or liquid, or of a mixed glutinous consistency. In Part II there is some interesting information regarding the movements in solid and fluid media; and in the last part we are informed that movements of translation are very feeble, and that it is not always possible to differentiate between these and the ordinary passive motility (rotation, bending and pendulum movements), which reaches a maximum on the twelfth day of the culture. The article is illustrated profusely with actual microphotographs. H. S.

THE FUNCTION OF THE CELLULAR INFILTRATION IN SYPHILITIC LESIONS, WITH THERAPEUTIC DEDUCTIONS. F. HERB. (*Urol. and Cut. Review*, June, 1923.)

"CELLULAR infiltrations reflect Nature's method of dealing with the particular disease," and this author avers that valuable therapeutic deductions can be drawn from a correct interpretation of their function. In syphilitic infiltrations there are three types of cells which characterise the lesion, viz. lymphocytes, plasma-cells, and fibroblasts.

These different cells, he states, must serve either of two objects: the destruction and disposal of the invaders, or the repair of tissue.

The fibroblasts are present to repair loss of tissue; the *rôle* of the lymphocytes and the plasma-cells is to dispose of the invaders. The plasma-cells, which have the necessary protoplasm, supply a lipase, a fat-splitting ferment that endows the plasma-cells with a spirochæticidal property. To the lymphocyte is left the function of supplying the complement, which the author believes is stored in the nucleus. In late syphilis there is a marked decrease of complement, consequently more and more lymphocytes are required to furnish to the ferments the same quantity of complement: hence the massive accumulation of lymphocytes in gummata.

Therapeutically it is important to appreciate that there are natural forces

in the body which can make or unmake the success of our remedies, and these natural forces, he states, are vested in the lymphocytic apparatus. The good effects of iodine and sodium nucleinate are due to the stimulation of the lymphocytic apparatus with the production of lymphocytosis. W. H. B.

THE SPECIFIC TREATMENT OF CHANCROIDS. ROSENWALD. (*Urol. and Cut. Review*, September, 1923.)

THE author records as specific the following method of treating chancroids:

The drugs are measured by volume: Calomel, 1 oz.; zinc sulph., 2 oz.; fluid camphorated opium, 2 oz.; lime-water, 8 oz. Saturate cotton-wool with the lotion and apply to chancroids.

The following day this is changed to an ointment composed of zinc oxide, 1 oz.; starch, 1 oz.; acid boric, 1 oz.; camphor, 1 oz.; 3 per cent. carbolised vaseline, 12 oz. This is applied daily. The sores heal rapidly according to the writer's experience W. H. B.

QUARTERLY SURVEY OF DERMATOLOGICAL LITERATURE.

ERYTHEMAS, INFLAMMATIONS, ETC.

Acrodermatitis Chronica Atrophicans and its Relation to Sclroderma. F. WISE. (*New York Med. Journ.*, 1923, cxviii. No. 2, p. 73.)

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Actinomycosis with Recovery. A. D. BIGLAND. (*Brit. Med. Journ.*, July 14th, 1923, ii, p. 61.)

Angioneuroses, Contribution to the Clinical Study of. F. FRICK. (*Med. Revue*, June-July, 1921, p. 241.)

Angio-neurotic Œdema with Adenopathy. Z. MORAVEC. (*Ceská Dermatologie*, 1923, iv, p. 91.)

Aplasia Moniliformis. J. STRANDBERG. (*Acta Dermato-venereologica*, iii. 3–4, December, 1922, p. 650.)

Cheilitis, Chronic Actinic. S. AYRES. (*Journ. Amer. Med. Assoc.*, October 6th, 1923, lxxxi, No. 14, p. 1183.)

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Dermal Leishmaniosis, Phosphorus Treatment. A. CASTELLANI. (*Journ. Trop. Med.*, June 1st, 1923, xxiv, p. 194.)

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Erythema Nodosum, Familial Cases. P. WORINGER. (*Journ. de Méd. de Paris*, 1923, xlii, xii, p. 241.)

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Erythrœdema Polyneuritis. D. Patterson and J. G. Greenfield. (*Quart. Journ of Medicine*, October, 1923, No. 65, p. 6.)

Frambœsia Tropica. Gislen. (*Arch. Med. Belges*, 1923, lxxvi, 6, p. 464.)

Fur Eruptions, Illustrated. R. Prosser White. (*Trans. Lond. Derm. Soc.*, 1923, p. 43.)

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Granuloma Inguinale, Report of a Case and Review of the Literature. Carter. (*Urol. and Cut. Review*, September, 1923.)

Granuloma Pediculatum. Falkenstein. (*Derm. Zeitschr.*, January, 1923, p. 299.)

Hereditary Pigmentation of the Leg with Atrophy. M. F. Engman. (*Arch. of Derm. and Syph.*, October, 1923, viii, p. 483.)

Herpes Zoster and Varicella. Johanna Schram Anderssen. (*Med. Revue*, August, 1923, p. 447.)

Herpes Zoster with Motor Paralysis of the Shoulder Muscles. K. Zeinher-Henriksen. (*Norsk Mag. f. Lægev.*, April, 1923, p. 411.)

Inflammation. L. Torok. (*Arch. of Derm. and Syph.*, October, 1923, viii, p. 505.)

Iodide and Bromide Exanthems. U. J. Wile. (*Arch. of Derm. and Syph.*, September, 1923, viii, No. 3, p. 407.)

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Nævus Unius Lateris with Lymphangiectatic Hypertrophy of the Vulva. N. Tobias. (*Arch. of Derm. and Syph.*, November, 1923, ix, p. 647.)

Oleic Acid Dermatitis, Case of. W. H. Harley. (*Arch. of Derm. and Syph.*, October, 1923, viii, p. 530.)

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Scleroderma Neonatorum. Christen Johanessen. (*Norsk Mag. f. Lægev.*, June, 1923, p. 560.)

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Urticaria Pigmentosa. C. W. Finnerud. (*Arch. of Derm. and Syph.*, September, 1923, viii, No. 3, p. 344.)

Veronal Poisoning, Rash in. I. J. Sands. (*Journ. Amer. Med. Assoc.*, November 3rd, 1923, lxxxi. No. 18, p. 1519.)

Vitiligo, Alopecia Areata and Severe Hyperthyroidism. S. Ayres. (*Arch. of Derm. and Syph.*, October, 1923, viii, p. 502.)

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Xanthoma Diabeticorum Treated with Insulin. M. F. Engman and R. S. Weiss. (*Arch. of Derm. and Syph.*, November, 1923, ix, p. 625.)

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Melanoma of Hand, Malignant. L. A. Sutton. (*Arch. of Derm. and Syph.*, September, 1923, viii, No. 3, p. 325.)

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Rongalit White Staining in Skin Histology. Pakheiser. (*Derm. Zeitschr.*, May, 1923, p. 263.)

TREATMENT.

Acne, X Ray *versus* Vaccine Treatment. H. Fox. (*Journ. Amer. Med. Assoc.*, October 27th, 1923, lxxxi, No. 17, p. 1417.)

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X-Ray and Combined Treatment of Acne Vulgaris. T. T. Eller. (*New York Med. Journ.*, 1923, cxviii, No. 1, p. 62.)

X-Ray Treatment of Skin and its Appendages. F. J. Stansfield. (*Med. Journ. of Australia*, September 1st, 1923, ii, No. 9, p. 217.)

SYPHILIS.

General.

Children, Acquired Syphilis in. M. A. Jaureguy. (*Arch. Lat.-Amer. de Pediatries*, February, 1923, xvii, p. 81.)

Defensive Mechanism of the Human Body in the Case of Syphilis. F. Herb. (*Urol. and Cut. Review*, September, 1923, p. 457.)

Neo-natal Mortality associated with Syphilis. A. B. Spalding. (*Journ. Amer. Med. Assoc.*, October 20th, 1923, lxxxi, No. 16, p. 1345.)

Orbit, Syphilis of. J. E. Kemp. (*Arch. of Derm. and Syph.*, August, 1923, viii, No. 2, p. 165.)

Pregnant Syphilitics. Pomaret and Benoit. (*Bull. et mém. Soc. Med. d'hôp. de Paris*, May 11th, 1923, xlvii, p. 699.)

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Treatment.

Bismuth in Syphilis. L. K. McCafferty. (*Arch. of Derm. and Syph.*, October, 1923, viii, p. 469.)

Dermatitis under Combined Mercury Neo-Salvarsan Treatment. Finn Hanssen. (*Med. Revue*, March, 1923, p. 213.)

Gelatin Arsphenamin and Disodium Arsphenamin. J. Oliver, E. Douglas and F. Kolos. (*Arch. of Derm. and Syph.*, September, 1923, viii, No. 3, p. 359.)

Hæmorrhages after Arsphenamin. P. Emile-Weil. (*Presse méd.*, July 28th, 1923, xxxi, p. 657.)

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Jaundice on the Rhine after Arsenobenzol. P. Power. (*Journ. Roy. Army Med. Corps*, November, 1923, xli, No. 5, p. 357.)

Potassium Iodide, Influence on Wassermann Reaction. Hirsch. (*Derm. Zeitschr.*, May, 1923, p. 273.)

Salvarsan Eruption, Spontaneous Relapse of. Harry. (*Derm. Zeitschr.*, January, 1923, p. 305.)

REVIEW.

Lectures on Diseases of the Skin.*

Dr. Wallace Beatty's *Lectures on Diseases of the Skin* have been published at the request of many of his past and present pupils, and to these the book cannot fail to be of great interest and value. It will appeal, too, to a wider circle, and particularly to readers of this Journal, to whom Dr. Beatty's name and work have been so well known for many years.

The Lectures are reproduced not quite in the usual form of discourses upon the subjects with which they deal, but rather as notes such as might have been made by an ideal student listening to the lectures, corrected and expanded by the author and embellished with aphorisms, with appropriate quotations from other writers, and with concise notes of illustrative cases from his case-books. They thus form a valuable record of Dr. Beatty's experience and method of teaching. They reflect the personality of the lecturer not only as a sound and scientific teacher, but, too, as an artist in dermatological therapy. Dr. Beatty emphasises the advice to study neatness and the comfort of patients, and the lectures abound with elegant and useful prescriptions and with careful details as to their proper employment. Among minor useful therapeutic hints we note that freezing (*e.g.* with anæstile) and curetting is recommended as an excellent treatment for warts and molluscum contagiosum. No scar is left. The lecture on the treatment of pruritus, general and local, is a good example of Dr. Beatty's sound therapeutic teaching.

It is interesting to read that rodent ulcer is regarded as a late developing nævus of sweat-gland-cell origin; that lupus erythematosus is thought to be of non-tuberculous origin; that pityriasis rosea (contrary to experience in London) is a comparatively rare affection; and that Recklinghausen's disease is so very rare that Dr. Beatty has never met with a perfectly developed instance.

The name "lichen axillaris" is suggested for Fox-Fordyce's disease, although, as the author observes, it may effect also the pubic region and the areolæ mammæ.

The lectures are preceded by a useful list of armamenta for clinical work and by a chapter on pathological technique, and there is an appendix on the principles of X-ray therapy by Dr. W. Geoffrey Harvey. H. G. A.

Lectures on Diseases of the Skin. By Wallace Beatty, M.D., F.R.C.P.I., Physician to the Adelaide Hospital, Dublin; Hon. Professor of Dermatology, Trinity College, Dublin. Pp. viii + 454. Dublin: Fannin & Co., Ltd., 1923. Cr. 8vo. Price 15*s.* net.

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